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GROUPING BEHAVIOR OF NORMAL PERSONS AND OF PERSONS WITH LESIONS OF THE BRAIN

FURTHER ANALYSIS

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AND
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CHICAGO

In an investigation of grouping behavior in patients with cerebral lesions and in normal persons, Halstead [1] found both quantitative and qualitative deviations from the normal in the performances of certain patients with cerebral injury. It was found, for example, that patients with a primary lesion in either the right or the left frontal lobe (1) employed fewer objects "spontaneously" from a field of 62 test objects in response to the instruction to place those together which "seem to belong together"; (2) recalled fewer objects after an interval of five minutes; (3) manifested little or no differential recall of grouped as opposed to ungrouped objects; (4) produced a smaller total number of groups, and (5) deviated characteristically in the distribution of the types of groups created, as determined by an adaptation of Klüver's method of equivalent and nonequivalent stimuli. This work, based on neurosurgical cases, seemed to indicate that various organizing principles, such as "shape," "size" and "color," employed in dealing with multiple objects or events may be rendered differentially available by damage to the brain.

In the present investigation further analysis has been made of grouping behavior in normal subjects and in persons with injury to the

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Read at the Ninety-Seventh Annual Meeting of the American Psychiatric Association, Richmond, Va., May 7, 1941.

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1. Halstead, W. C.: (*a*) Behavioral Effects of Lesions of the Frontal Lobe in Man, Arch. Neurol. & Psychiat. **42**:780-783 (Oct.) 1939; (*b*) Preliminary Analysis of Grouping Behavior in Patients with Cerebral Injury by the Method of Equivalent and Non-Equivalent Stimuli, Am. J. Psychiat. **96**:1263-1294, 1940.

brain. The test situation in this investigation differed in certain essentials from that previously employed by Halstead: (1) Geometric figures were used in place of actual objects; (2) the test figures were presented serially to the subject by means of a special apparatus, and (3) the subjects worked with a knowledge of their "successes" and "failures" (since the apparatus was set to respond to "correct" choices only).

APPARATUS, TEST MATERIALS AND PROCEDURES

Apparatus.—The apparatus consisted essentially of an electrically controlled exposure device for serial presentation of groups of two dimensional test figures and an associated keyboard providing a multiple response situation for the subject. Each correct response of the subject automatically resulted in the presentation of another set of test figures by the apparatus.

The test figures for each test employed were prepared on a separate strip of white holland cloth, which in operation was attached to the outer circumference of a metal drum. An electrical escapement mechanism, controlled by a bank of four switches located below a viewing window, activated the drum in stepwise fashion about its horizontal axis. A limiting aperture and the viewing window placed before the drum restricted the field to the test figures of a single item for any given position of the drum. As brought to sharp focus by a 2.5 power reading lens, the test figures averaged approximately 3 by 3 degrees of visual angle bidimensionally for the subject.

Incorporated in the apparatus was a stylograph, with five signal magnets. One signal magnet corresponded to each release switch, and each magnet registered a signal every time the corresponding switch was thrown, regardless of whether or not the switch was in the effective tripping circuit at the moment. The fifth signal magnet registered a signal every time the release mechanism was activated. The stylograph paper, driven by a synchronous motor, provided a graphic record of the operation of every switch, the order in which the switches were operated, the "correctness" of the response and the partial and total time intervals involved.

Test Materials.—In devising the test materials our general purpose was to present groups of test figures that would normally be dealt with spontaneously in terms of certain categories or organizing principles.

A photograph of the test figures comprising the 9 tests, adopted as a standard series after considerable preliminary work with normal subjects and a number of subjects with cerebral lesions is presented in figure 1. The following brief description of the various tests requires frequent reference to figure 1.

TEST 1.—Roman Numerals: This test is intended to serve primarily as a practice test which would make it possible to keep verbal instructions at a minimum. Each Roman numeral of test 1 corresponds to the number of the key which operates the machine for that trial. For example, in the first item of test 1 the Roman numeral I can be seen through the viewing aperture. The "correct" response of the subject consists in throwing the switch which is labeled I. When this is done the second item of test 1, the Roman numeral III, is exposed. When the subject operates the switch labeled III, the mechanism is tripped and the next item is exposed, etc. The four switches are labeled from the left to the right, with switch I placed at the subject's left as he views the test items.

TEST 2.—Number of Objects: In general, an effective cue to the "correct" key is provided by the number of objects or signs present in any given test item. For example, the four manikins in the eighteenth test item indicate that the fourth key is to be pressed, and the three plus signs opposite number 28, in the left column, indicate the third key. (The interpretation of figure 1 will be clearer if it is remembered that the key indicated by any given Roman numeral of test 1 is also the correct key for all presentation items on the same horizontal line;

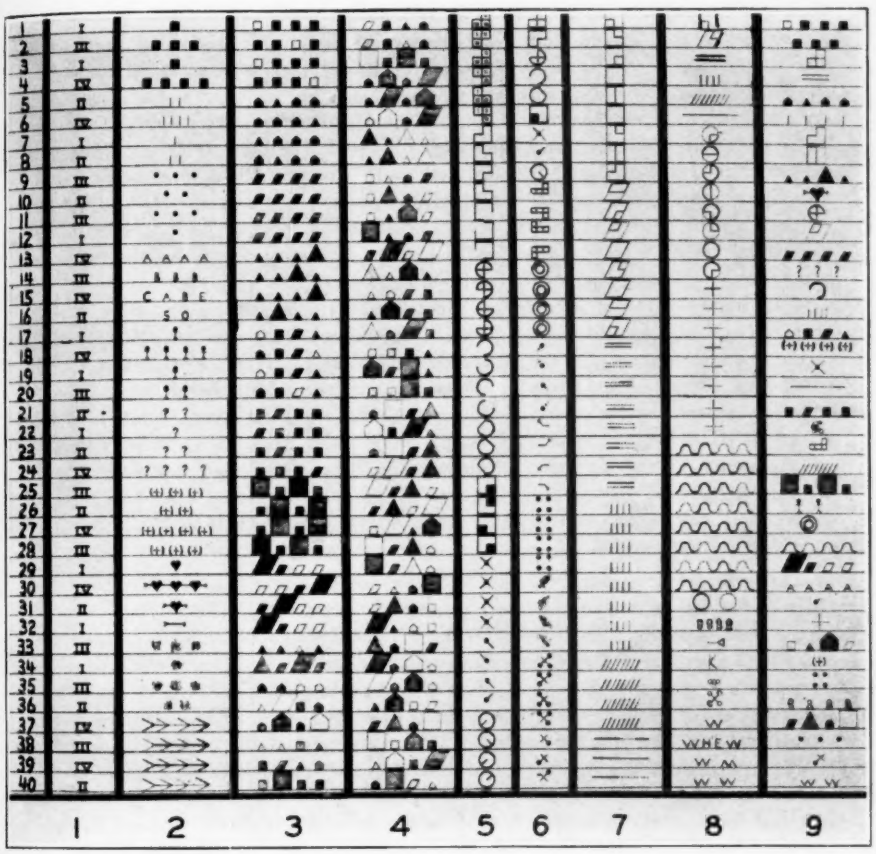

Fig. 1.—Photograph of test figures, reduction × 5. The 40 items of each numbered vertical column constitute an individual test. Each item was exposed separately (see text). The correct key or switch (of four) on the multiple choice apparatus corresponding with the items of each of the 9 tests (i. e., the horizontal rows above) also corresponds with the Roman numeral test figures of test 1.

that is, the same key corresponds to all test items opposite any given arabic numeral. Hereafter we shall refer to the test items by number; e. g., the letters SO in test 2 will be referred to as item 16, test 2.) Items 37, 38, 39 and 40 in test 2 were composed of red and black lines in the original test material. It was

intended that the number of black lines in any one of the arrow-like figures should serve as an effective cue—two black lines: the second key, etc.

TESTS 3 and 4.—Oddity: These tests may be designated as oddity tests. One of the four figures in each presentation space differs from the three others in a certain characteristic, and the position of the odd figure gives the clue as to the correct key. Oddity always occurs in one of four characteristics: solid outline (items 1 to 4, 17 to 20, 33 and 37 in test 3, and items 1 to 3, 13, 17, 21 to 23, 33 and 37 in test 4); shape (items 5 to 8, 21 to 24, 34 and 38 in test 3, and items 4 to 6, 14, 18, 24 to 26, 34 and 28 in test 4); color [2] (items 9 to 12, 25 to 28, 35 and 39 in test 3, and items 7 to 9, 15, 19, 27 to 29, 35 and 39 in test 4), and size (items 13 to 16, 29 to 32, 36 and 40 in test 3, and items 10 to 12, 16, 20, 30 to 32, 36 and 40 in test 4).

The items of these two tests are graded in difficulty. The odd figure in the items of the first part of test 3 is perceptually striking. As one proceeds through the latter part of test 3 and then through test 4 the perceptual prominence of the odd figure diminishes, and for continued correct responses this test seems to demand a shift toward a logical–verbal procedure in discovering the odd figure. Perceptual oddity is progressively obscured in successive exposures during these two tests by the introduction of additional characteristics. If one considers the first 16 items of test 3, one finds that if oddity is present in the solid outline characteristic, the figures are all alike in color, size and shape; if oddity occurs in the shape characteristic, the figures are all alike in color and size and are all solid, etc. Items 17 to 40 in test 3 all contain one additional feature; i. e., if oddity is present in the shape characteristic, there are differences in the figures in one of the other characteristics (e. g., color, items 21 to 24; size, item 34); if oddity occurs in the size characteristic, differences exist among the figures in respect to color, shape or solid outline. In the first part of test 4, additional differences are present in two features, and in the last part of test 4 all four variables are represented in each item, but true oddity occurs in only one.

TESTS 5 and 6.—Quadrant: Each figure includes a characteristic which signifies or points to one of the four possible quadrants. The quadrants are arbitrarily numbered in a clockwise direction, beginning with no. 1 at the upper left. In order successfully to complete these tests the subject must grasp the principle of quadrantic arrangement and must further associate each of the four quadrants with one of the four keys. The quadrant arbitrarily numbered I corresponds to the first key; the quadrant number II corresponds to the second key, etc.

The cue embodied in the items of tests 5 and 6 is quite unmistakable, except in items 29 to 32, test 5, and figures 10 to 13 and 26 to 29, test 6. The central disk and three of the radiating lines in items 29 to 32, test 5, are green, whereas the fourth radiating line is black. The fourth black line indicates the significant quadrant. The correct cue is obtained from items 10 to 13, test 6, by regarding the fourth offset square as being situated in one of the four quadrants. Items 26 to 29, test 6, contain three green disks and one black disk. The color difference is not well represented in figure 1, although the reader can infer the position of the black disk from the knowledge that its position indicates the significant quadrant.

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2. The colors used in the original test materials (black, red, green, blue and orange) are reproduced as shades of gray in figure 2. By knowing which key is the correct one for each of the items in tests 2 and 3 (compare test 1) significant color differences in specific figures may be inferred.

TESTS 7 and 8.—Part-Whole: Key I is indicated if one fourth of the figure, or of the number of lines, is composed of solid lines, the remainder consisting of dotted lines. If one half is in solid lines, key II is indicated; if three fourths is solid, key III is indicated, and if the entire figure (or all the lines) is solid, key IV is correct.

TEST 9.—Recognition: The final test was made up of a selection of items taken from tests 2 to 8. The material in test 9 is identical with or similar to corresponding items in the other tests.

Procedure.—The procedure consisted essentially of securing "spontaneous" responses of the subject to the 40 test items in each of the 9 tests described in the foregoing section. Each test was presented separately and in numerical sequence from test 1 through test 9.

The subject was seated in front of the apparatus, the height of which was then adjusted to permit full and clear vision of the presentation material. With item I of test 1 present in the viewing aperture, brief instructions were given:

"You have seen switches like this before. They are ordinary light switches [examiner turns the four switches on and off in succession]. The machine isn't running now; so nothing happens when I turn on the switches. Now I turn on the machine. Now, if you press the correct key, this figure which you see [examiner points to viewing window] will disappear, and something else will take its place. Then, again, if you press the correct key, there will be another change, and so on. Each time, only *one* of the four keys will make it move. If you press any of the three wrong keys, nothing will happen; so you will know whether or not you were right. Now, what you see in here always tells you somehow which key is the right one. It gives you a clue or a hint, and what I want you to do is to try to discover the nature of that clue or hint. If you discover it, you will be able to press the right key every time—to make the figure move every time you press a key. You can take all the time you want. The object is to press the right key as often as possible."

In giving these instructions, an effort was made to suit the language of the instructions to the subject. Questions coming from the subject were answered insofar as they bore on the foregoing instructions. Frequently the subject asked whether the number I that he saw meant that he should press a certain key, and then he was told that that was exactly what we wanted him to determine. Subjects were allowed to continue unaided in their solutions of the tests, within the time limit set by the experimenter. Whenever the experimenter undertook to aid the subject, he proceeded by giving at first vague hints and by making more and more obvious suggestions as the subject's performance failed to improve. A careful record was kept of all helps which were given. In some cases the conversation between the experimenter and the subject, during part or all of an experimental session, was recorded on a phonograph. Whenever this was done, the subject was encouraged to verbalize freely.

SUBJECTS

Normal Control Subjects.—The results obtained with a group of 10 normal subjects form the basis for the graphic presentation of results for normal persons as indicated in figures 3 to 8. This group was heterogeneous as to age, sex, educational background and socioeconomic status. All control subjects were in good general health at the time they were tested and were selected primarily from the standpoint of availability.

Experimental Subjects (neurosurgical patients).—The results obtained on 6 neurosurgical patients from the series previously reported by Halstead [1b] constitute the basis for the graphs of individual performances in figures 3 to 8. Before these results are considered, attention should be directed to the following facts concerning the experimental subjects: These operative patients represented unusually "good" or "successful" recoveries. Each patient presented only minimal local signs (if any) of the neurologic lesion; each had resumed gainful occupation or studies (in 2 instances at the college level) or preparations to that end. Each patient was in excellent general health at the time of testing. (The limits of formal intelligence were established after operation by means of one or more standard intelligence tests.) Excellent rapport during the tests had developed over a period of months or years, during which each subject had cooperated voluntarily with this laboratory in studies involving a wide range of behavior functions.

Diagrams indicating the minimal cerebral lesions for each of the 6 experimental subjects (subjects 1, 6 10, 19, 22 and 25) are presented in figure 2. The diagrams were prepared in the manner previously described by Halstead.[1b]

RESULTS

The number of errors made on the first attempt in each of the 9 tests provides a quantitative basis of comparison between the performances of the experimental subjects and those of the normal control group. Because of the relatively low variability in the performances of the normal subjects, the average performance of the group on each of the 9 tests has been taken as a point of reference in presenting individual profiles of the experimental subjects.

Normal Subjects.—All the 10 control subjects "spontaneously" discovered the solution in all 9 of the standard tests (fig. 2) during the first trial. This was true in spite of the fact that none of these subjects received aid or suggestions on any of the items and that the concepts employed by the subjects in solving some of the tests needed to be progressively refined or broadened to permit continued successful responses. Deviations from subject to subject in approach to the tests tended to be minor in character with reference to the total results and need not be examined here in detail.

Experimental Subjects (neurosurgical patients).—The 6 subjects who had undergone operation were from the series reported previously by one of us (Halstead [1b]). In the interest of continuity the same case numbers (1, 6, 10, 19, 22 and 25) are employed here.

Subject 1.—An American-born man aged 48, a salesman, entered the University of Chicago Clinics on Sept. 4, 1935 with a history of severe headaches, occasional vomiting, blurred vision and loss of weight. Operation, performed on September 17 by Dr. Percival Bailey, involved partial extirpation of the left prefrontal lobe for removal of a meningioma of the olfactory groove. Recovery was uneventful; the patient was discharged from the hospital on September 28.

The postoperative intelligence quotient was 110 (Stanford-Binet). The patient was strongly "right handed." Postoperative social adjustment included phenomenal "success" as a salesman.

In figure 3 the number of errors made by subject 1 on the first trial of each of the tests (completed by him) is shown graphically. The solid horizontal black line indicates the average score on each test made by the group of normal subjects; the vertical lines indicate the average variations in the normal group for the 9 tests.

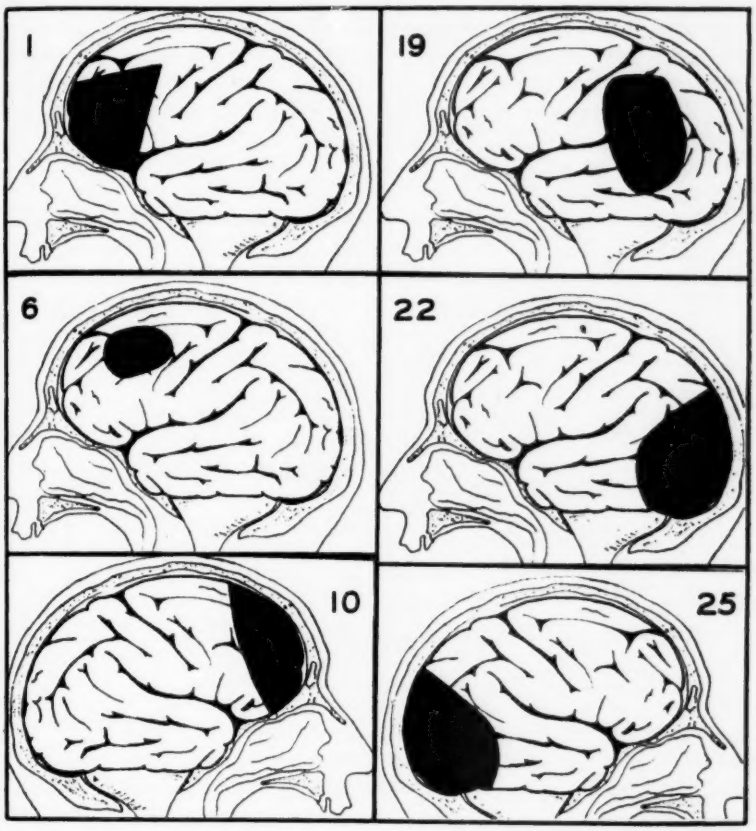

Fig. 2.—Diagrams indicating the approximate lesion (in its lateral aspect) of each of the experimental subjects. These diagrams were prepared by the method described by Halstead.[1b] Lesions in the left hemisphere are indicated by the case number in the upper left corner of each diagram; lesions in the right hemisphere, by the case number in the upper right corner.

Quantitatively, the most striking feature of the performances of subject 1 is the fact that, with the exception of test 3, all of his scores fell outside the limits of the normal group. (His performance on test 3 indicates, however, that he could manifest a normal grasp of the task imposed by that test.) He encountered considerable difficulty at the outset with test 1. He appeared to grasp the

instructions; he selected one key after another after deliberate study of the particular figure in the window and yet did not grasp at once the fact of simple and never failing correspondence of identity between the number appearing as the figure in the window and the number of the "correct" key. During the first half of the test he appeared to have adopted an attitude of "trial and error" searching and yet gave no evidence that such experience could subsequently be utilized in solution of the general problem. This attitude was common to the normal subjects, but experience with one or two items was usually sufficient for the principle of "identical number" to emerge. After a series of errors in test 1, the subject (S) complained that the experimenter (E) was expecting "quite a bit" from some one who had been out of school a long time. The following conversation then ensued:

E: "When you get on to it you will be surprised how simple it really is."

S (looking at the figure in the window of the apparatus).: "Well, now, there is number IV, but it wouldn't be the fourth key."

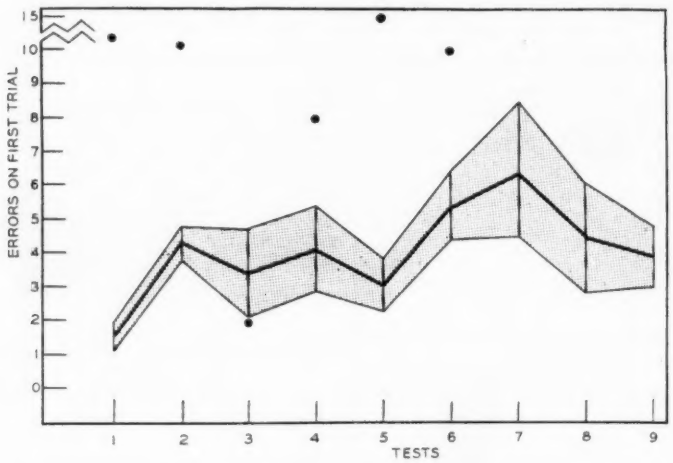

Fig. 3.—Graph indicating the performance of subject 1 (lesion in the left frontal lobe), showing the number of errors (black dots) made on the first trial on 6 of the 9 tests. The average performance of the normal control subjects in each of the tests is indicated by the profile in the lower portion of the figure (heavy black line). The average deviation of the normal subjects in each test is indicated by the limits of the shaded area.

E: "Why wouldn't it be the fourth key?"

S: "I tried that system before, but it didn't work."

Subject 1 thereupon tried key IV, which proved to be "correct." He then completed test 1 without further errors.

Soon after commencing test 5 subject 1 announced that he had discovered the solution—"the number that is missing." He used this clue successfully as long as there were three numbers and a fourth number was missing, i. e., until he came to the seventh item, which did not include any numbers and hence was not characterized by a missing number. It did not seem to occur to him that there was any kind of continuity between the first six items and the succeeding ones.

The aid offered by the examiner was at first confined to the repeated assertion that a single principle would apply to and permit the solution of all the items in the test. The subject continued to make errors, however, and the experimenter finally suggested the quadrant principle to him. From the nature of further errors made by subject 1, it was apparent that he was proceeding on the assumption that both the upper and the lower pair of quadrants should be numbered from left to right. He expressed the view, when questioned, that any other number arrangement would be wrong. Since his expressed conviction was so strong as to make it improbable that he would spontaneously entertain any other possibilities, the clockwise manner of numbering was specifically explained to him. He finally grasped the correct principle and then proceeded to utilize it as effectively as any other subject throughout the remainder of the test.

At the conclusion of test 6, subject 1 declined to continue with the remaining tests. The only reason that he would offer was: "That machine's got me buffaloed." Attempts made subsequently to get him to complete the tests drew the same answer. It is of interest that this test situation and the Rorschach situation provided the only 2 instances of refusal of a test situation out of several hundred hours of study of subject 1 during the past five years.

SUBJECT 6.—An American-born man aged 51, of Irish descent, a traffic policeman, entered the University of Chicago Clinics on June 17, 1936 with a history of severe headaches, spells of dizziness and unsteadiness for the past four months and progressive failure of memory. Operation, performed on June 17 by Dr. Paul C. Bucy, involved partial extirpation of the left prefrontal lobe for removal of benign glioma of the septum pellucidum. Recovery was uneventful, and the patient was discharged from the hospital on July 20. The postoperative intelligence quotient was 105 (Stanford-Binet). The patient is strongly "right handed." He is a retired bachelor with a modest but comfortable income from his savings and pension. He spends his time "enjoying life" in conventional ways.

Subject 6 began test 1 (fig. 4) by systematically operating the keys in the order: 1, 2, 3, 4; 1, 2, 3, 4, etc. His statement of the solution of the test was, "It goes in a rotating fashion," and he seemed to feel that he had accomplished what was expected of him. The experimenter then emphasized that the subject was to try to make the machine trip every time he pressed a key. The subject seemed at first unable to do this, but after being questioned item by item by the experimenter in terms of "What do you see? Now which key are you going to press?" he grasped the solution and was able to utilize it without further errors. In test 2 subject 6 encountered no particular difficulty until he reached item 30, the three hearts and an arrow. Then he leaned back in his chair and studied the figure. He seemed unwilling to proceed. The following conversation ensued:

E: "What do you have there?"

S: "Three hearts."

E: "Is that all?"

S: "No; there's a string through them."

E: "Oh, three hearts and a string?"

S: "Yes."

E: "Well, could that be four things then?"

S: "Yes. Well, I suppose it's this key there" (subject chooses key IV, the "correct" key).

Subject 6 was then able to count the heart and the arrow in item 31 as two figures and to respond on that basis. On reaching item 37, the subject again

appeared unwilling to proceed further, complaining that he knew of no way to deal with the figure. It was then pointed out that the arrow-like figure could be regarded as composed of nine individual lines, that some of these lines were black and some were red and that it was possible to count separately the number of black and the number of red lines. Then, during the subject's effort with items 37 to 40, he was asked for each item: "How many black lines? Then which key are you going to press?" The "coaching" seemed to enable the subject to grasp the solution of the arrow-like figures.

In test 5 (quadrant) subject 6 encountered considerable difficulty. When the experimenter realized that the subject did not grasp the quadrant principle, he

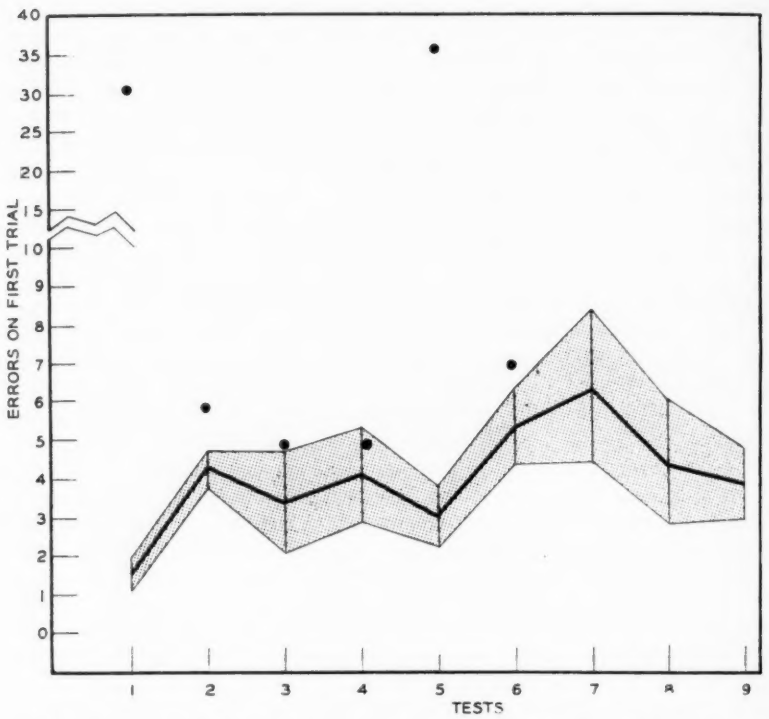

Fig. 4.—Graph indicating the performance of subject 6 (lesion in the left frontal lobe), showing the number of errors (black dots) made on the first trial in 6 of the 9 tests. The profile in the lower portion of the figure represents normal variation in each test and is the same as that in figure 3.

called it to the latter's attention. This did not improve the subject's performance, however. Finally the examiner prepared a diagram, a square divided into four parts, with Roman numerals in each quadrant. The diagram and its relation to the tests were explained. The subject was then able to solve the next few items with the aid of the diagram; when each new item appeared, he consulted the diagram and then chose the correct key. Next he was encouraged to attempt the solution without the diagram, which he was unable to do. As a last help, the examiner spoke to the subject as follows: "Can you imagine the window [pointing

to the viewing window] to be divided into four parts? Now can you imagine the number I to be here in the upper left, the number II in the upper right, the number III in the lower right and the number IV in the lower left?" At this point subject 6 seemed to grasp the principle and then completed the remaining items of test 5 without error.

As in the case of subject 1, test 6 (quadrant) was the last in the series to be completed by subject 6. He insisted that the tests were too difficul' and strongly urged that he not be asked to do more of them.

SUBJECT 10.—An American-born woman aged 31, a housewife, entered the University of Chicago Clinics on July 24, 1939 with a history of severe throbbing headaches and numbness and tingling of the upper and lower extremities during the past six months. Operation, performed on July 29 by Dr. A. Earl Walker, involved partial extirpation of the right prefrontal lobe for removal of a cerebral

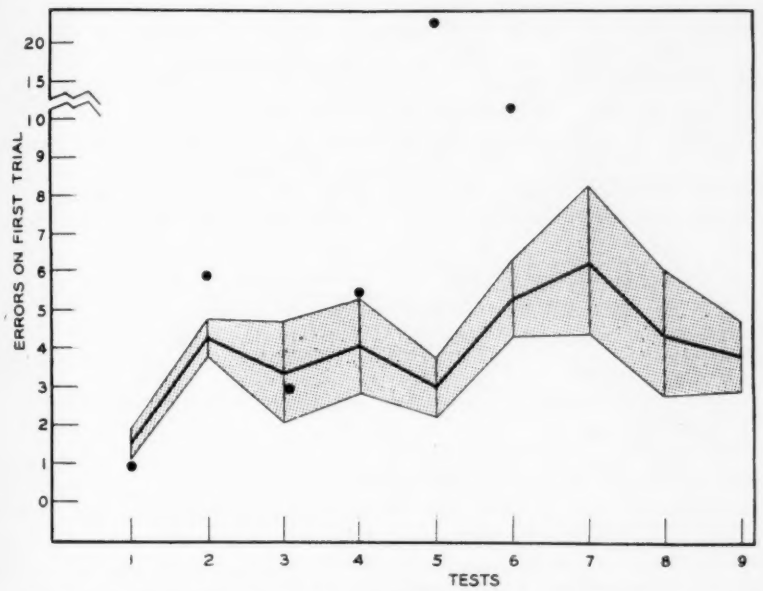

Fig. 5.—Graph indicating the performance of subject 10 (lesion in the right frontal lobe), showing the number of errors (black dots) made on the first trial in 6 of the 9 tests. The profile in the lower portion of the figure represents normal variation in each test and is the same as that in figure 3.

aneurysm. Recovery was uneventful, and the patient was discharged from the hospital on August 15. The preoperative intelligence quotient was 120 (Stanford-Binet), and the postoperative quotient was 124 (Stanford-Binet L). The patient is strongly "left handed." She manages a home with two children and a partially invalided husband, much as she did prior to her operation.

The general approach of subject 10 to the test situation in terms of prompt grasp of the instructions, general attitude and general mode of procedure in the first part of the series of tests could not be distinguished from that of the normal subjects. In test 5 (quadrant), however, she encountered considerable difficulty (fig. 5), making a total of 23 errors, as compared with the average of 3 errors

made by the normal subjects. In spite of the fact that the principle of the test was explained to her by means of a diagram, her performance did not materially improve.

On test 6 (quadrant) subject 10 made twice as many errors as the average normal subject in spite of the fact that the quadrant principle had been explained in test 5. The general nature of subject 10's performance may be illustrated with reference to items 18 to 20. These items, each composed of three dots of decreasing size, were normally usually envisaged as pointing in the direction of one of the quadrants made effective in the preceding items. Some of the normal subjects were uncertain, on first encountering these items, as to which of two diagonally opposite quadrants the dots might indicate, but all of the normal subjects were able to discover the correct solution in a short time and without aid. Subject 10, on the other hand, was at first unable to think of any way of dealing with these figures. Item 18 was resolved after trial and error had eliminated all keys but the correct one, but no possible explanation occurred to the subject. On item 19, the experimenter ventured to help to the extent of asking the subject how the item differed from the previous one. The fact that the subject was able to say, "They're the same, but reversed" did not suggest to her an interpretation in terms of the quadrant principle. The first hypothesis that suggested itself to the subject came when she was attempting to deal with item 19. She suggested that it might be key IV because "the large dot could contain four small ones."

When the subject showed no sign of discovering the solution by the time item 21 was reached, the experimenter undertook to offer help. This conversation took place:

E: "Before this you worked on the idea of four corners."

S: "Yes, but here I don't have four corners."

E: "Could you consider that they point in a certain direction?"

S: "Yes."

The subject then chose the correct key and said, "They work out when you consider them that way."

At the request of the subject, the series was terminated with test 6. She was considerably disturbed with her performance. In spite of the fact that repeated assurance was given that she had "done well," she voiced dislike for the tests and stated that she wanted to "stay away from them."

Subject 19.—An American-born youth aged 19, a student, entered the University of Chicago Clinics on Jan. 15, 1936 with a history of a fall at the age of 5 years, which resulted in a compound depressed fracture of the skull, repaired by operation. After the fracture, the patient was unable to speak for one week; he experienced severe weakness of the right arm and leg, which continued. Generalized jacksonian seizures began at the age of 13 years, and these persisted. Operation, performed on January 24 by Dr. Paul C. Bucy, involved partial extirpation of the left parietal and temporal lobes for removal of a cortical scar. Recovery was uneventful; the patient was discharged from the hospital on February 11. The postoperative intelligence quotient was 110 (Stanford-Binet L). The patient was strongly "right handed" in childhood, but weakness of the right arm and hand had necessitated the development of functional "preference" for the left hand. He was graduated from a large metropolitan high school after his first operation and at present is a student in an art school. He has occasionally shown "spiking" and 3 per second waves in his electroencephalogram, but these were not present at the time of the last determination.

As may be seen in figure 6, subject 19 made fewer errors than the average normal subject on 6 of the 9 tests. He grasped the instructions at once and made no errors on test 1. He worked slowly and deliberately, with no help from the experimenter. He expressed a lively interest in the tests and has since cooperated readily in repeating the tests. It should be noted that, in contrast to the preceding subjects, subject 19 had a visual field defect (right homonymous hemianopia of *vue nulle* type [2a]), in addition to defective ocular movements.[3] In general, his performance on the series of tests was superior to that of any of the normal subjects.

SUBJECT 22.—An American-born woman aged 25, a filing clerk, entered the University of Chicago Clinics on Sept. 27, 1937 with a history of visual disturbances during the past ten years, consisting of flickering lights and colors, and headaches and spells of vomiting for the past eighteen months. Operation, performed on October 23, by Dr. Paul C. Bucy, involved complete extirpation of the left

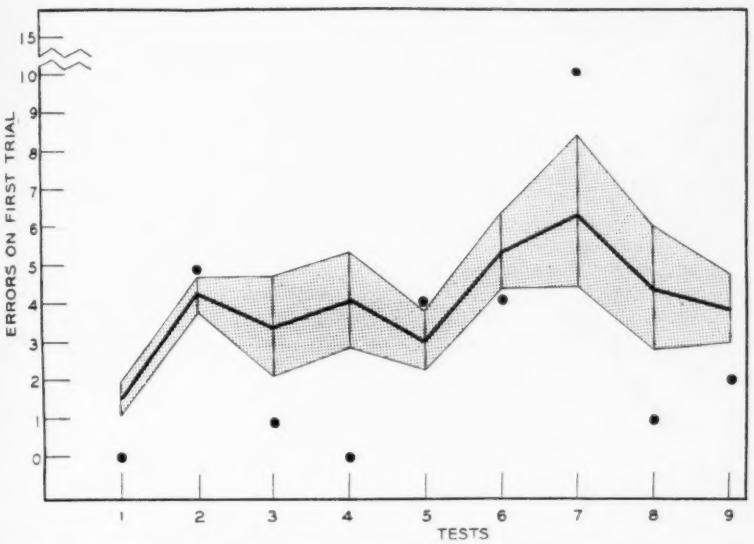

Fig. 6.—Graph indicating the performance of subject 19 (lesion in the left parietotemporal region), showing the number of errors (black dots) made on the first trial in each of the 9 tests. The profile in the lower portion of the figure represents normal variation in each test and is the same as that in figure 3.

occipital lobe for removal of a spongioblastoma polare. Recovery was uneventful, and the patient was discharged from the hospital on November 11. The postoperative intelligence quotient was 115 (Stanford-Binet). The patient was strongly "right handed." She secured employment for herself in a factory after her operation and has worked steadily since.

As may be seen in figure 7, subject 22 had only normal difficulty with test 1. She grasped the instructions promptly and, after making two errors at the outset,

2a. *Vue nulle*, as opposed to *vue noire*. No scotomatous area was present.

3. Halstead, W. C.: A Method for the Quantitative Recording of Eye Movements, J. Psychol. **6**:177-180, 1938.

proceeded without making further errors on this test. Likewise, her performance on tests 8 and 9 did not differ greatly from the average normal performance. Her performance on the intervening tests differed widely from the normal, however. In contrast to subjects 1, 6 and 10, the errors made by subject 22 did not seem to disturb her in the least. She worked steadily at each of the tests, seeking no assistance from the experimenter. She was permitted to go through all 9 tests without assistance of any kind. Her interest and attitude toward the tests did not differentiate her from the normal subjects. An analysis of various visual functions of subject 22 has been reported by one of us (Halstead) elsewhere.[4]

Subject 25.—An American-born woman aged 22, a stenographer, entered the University of Chicago Clinics on Sept. 27, 1939, with a history of severe head-

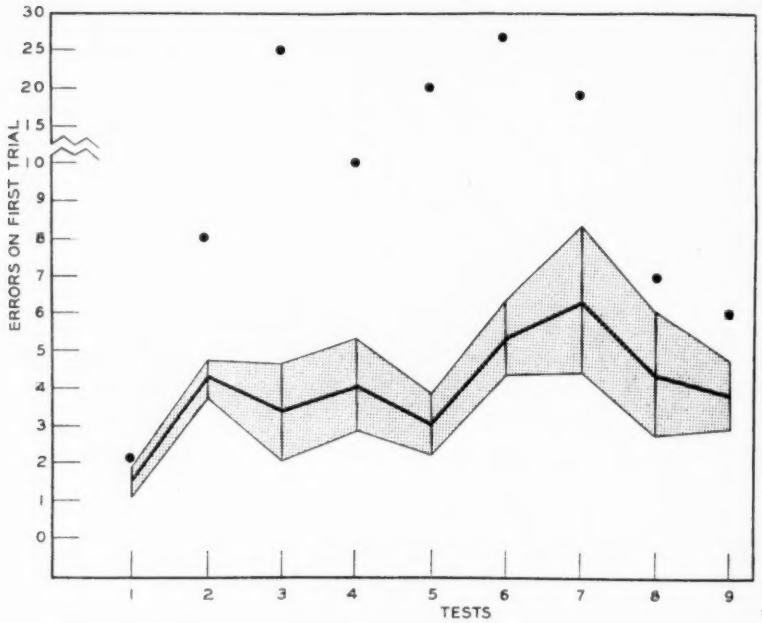

Fig. 7.—Graph indicating the performance of subject 22 (left occipital lobe completely removed), showing the number of errors (black dots) made on the first trial in each of the 9 tests. The profile in the lower portion of the figure represents normal variation in each test and is the same as that in figure 3.

aches and attacks of nausea, relieved by induced vomiting, during the past three years. Operation, performed on October 10 by Dr. Paul C. Bucy, involved complete extirpation of the right occipital lobe for removal of an oligodendroglioma. Recovery was uneventful, and the patient was discharged from the hospital on November 3. The preoperative intelligence quotient was 133 (standard-Binet L);

4. Halstead, W. C.; Walker, A. E., and Bucy, P. C.: Sparing and Nonsparing of Macular Vision Associated with Occipital Lobectomy in Man, Arch. Ophth. **24**:948-962 (Nov.) 1940.

the postoperative intelligence quotient was 133 (Stanford-Binet M). The patient was strongly "right handed." After her operation she resumed her secretarial duties in the office of a large corporation in Chicago. She was given additional responsibilities from time to time and an increase in salary. She is at present a student in a university.

It was possible to secure both preoperative and postoperative information in all 9 tests with subject 25. The two test periods were separated by an interim of six weeks. In figure 8 the preoperative results for this subject are plotted in solid dots and the postoperative results in hollow circles.

In the preoperative tests subject 25 grasped the instructions promptly and made only one error on test 1. She made 9 errors on test 2, as against an average of 4 errors for the average normal subject. She did not seem to be disturbed by her errors and worked steadily without seeking or receiving any assistance from the examiner. Her performance on test 3 fell within normal limits, and on test 4

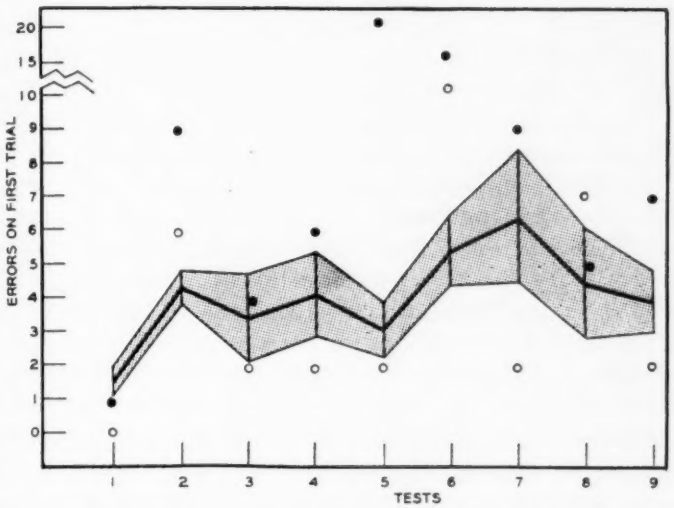

Fig. 8.—Graph indicating the preoperative (black dots) and postoperative (hollow circles) performance of subject 25 (right occipital lobe removed), showing the number of errors made on the first trial in each of the 9 tests. The profile in the lower portion of the figure represents the normal variation on each test and is the same as that in figure 3.

it was not notably different from the normal. She encountered considerable difficulty with tests 5 and 6 (quadrant), making 21 errors on the former and 16 errors on the latter. It is of interest that on the remaining tests, 7, 8 and 9, the performance of this subject was not notably differentiated from the average normal performance.

In the postoperative tests, with the exception of test 6 (quadrant), subject 25 encountered no particular difficulty, and in 6 of the 9 tests made fewer errors than the average normal subject. An analysis of various visual functions of subject 25 has been reported elsewhere.[4]

COMMENT

In the present investigation, we have been interested in the question whether certain forms of equivalence (in visually controlled responses) found in normal subjects likewise occur in persons with lesions of the brain. We were only incidentally concerned with determining the nature of the factors responsible for equivalence. Studies directed at the latter problem have been under way for some time in this laboratory. It seems clear that an adequate description of these factors for man requires intensive study of a wide range of behavioral functions in individual cases.[5] Certain features of the present investigation bear directly on any preliminary interpretation of the variations from normal performance found in some of the patients with cerebral lesions and may be mentioned briefly.

1. *Visual Acuity for Form, Brightness and Color.*—Careful determinations of the visual acuity for form, brightness and color in all 6 of the experimental subjects have been made by the methods reported in connection with an analysis of the visual functions of subjects 22 and 25.[4] No significant deviation from the normal was found in any of the 6 subjects with lesions of the brain which bore directly on their performances in the present investigation. The minimal visual form discrimination required in the test figures (which averaged approximately 3 by 3 degrees in size) subtended approximately 4 minutes of visual angle, a value well above the discrimination thresholds found for all 6 experimental subjects. Moreover, analysis of the errors made by the individual subjects indicates that relatively few errors were made on these particular figures.

2. *Visual Field Defect.*—Three of the 6 experimental subjects had a visual field defect associated with their cerebral lesion. Subjects 19 and 22 each had right homonymous hemianopia (with sparing of central vision) of *vue nulle* type.[4] Subject 25 had left homonymous hemianopia (with splitting of central vision) of *vue nulle* type.[4] It is of interest that of the 3 subjects with hemianopia, the performance of subject 19 was in general superior to that of any of the normal subjects (fig. 6). Likewise, the postoperative performance of subject 25 tended in general to equal or exceed the performance of the average normal subject. It thus seems improbable that the presence of hemianopia per se constituted the limiting factor in the performance of subject 22. This interpretation is further supported by an analysis of the errors made by this subject (fig. 7).

3. *Agnosia, Apraxia and Aphasia.*—Examinations of the language functions of all 6 experimental subjects have been made, including the

5. Klüver, H.: The Study of Personality and the Method of Equivalent and Non-Equivalent Stimuli, Character & Personality **5**:91-112, 1936. Halstead.[1b]

application of Head's tests and Halstead's test for aphasia, which covers twelve language functions, including agnosias and apraxias.[6] In general, no evidence of disturbed language functions was obtained for any of the 6 experimental subjects which would throw light at this time on the deviations from normal performance obtained in the present investigation. Four of the 6 subjects (subjects 10, 19, 22 and 25) indicated a normal grasp of the verbal instructions, accurate perception of the test figures and the ability to make the required responses by equaling the average normal performance on test 1. Two of the 6 subjects (subjects 1 and 6) made 11 and 30 errors, respectively, on test 1, as compared with 1 or 2 errors made by the average normal subject. Nothing in the general behavior of these 2 subjects suggested failure to grasp the instructions. Both subjects began test 1 promptly and activated the response keys differentially after deliberate study of the test items in the viewing window. It was only after several consecutive errors that it became apparent to the experimenter that they had not grasped the specific point of test 1.

4. *Attitude and Persistence.*—All 6 of the experimental subjects evidenced an interested, "cooperative" attitude at the outset of the tests. Subjects 19, 22 and 25 worked readily and persistently throughout the 9 tests without requiring special motivation from the experimenter. Subjects 1, 6 and 10, on the other hand, exhibited signs relatively early in the tests that their willingness to continue was marginal indeed. It was this fact that led the experimenter to give them direct assistance. In the case of each of them, this "resistance" to the tests seemed to wax and wane as errors or correct responses were made. On reaching the end of test 6, each of them substantially refused to proceed further with the tests, an attitude which remains to the present. This is of particular interest in connection with Goldstein's[7] description of the catastrophic reaction induced by certain test situations.

5. *Nature of the Tests.*—With the exception of subject 19, all of the experimental subjects had considerable difficulty with 1 or both of the quadrant tests (tests 5 and 6). It is of interest that the quadrant figures were the only test figures requiring a changing orientation to a vertical dimension of space. However, the performance of subject 1, for example, should be recalled in this connection: It was necessary for the experimenter to overcome an a priori conviction on the part of subject 1 that the quadrant test figures should be numbered from left to right rather than clockwise, as in the test.

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6. Halstead, W. C.: A Test for Aphasia, to be published.

7. Goldstein, K.: Die Lokalisation in der Grosshirnrinde, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10, pp. 600-842.

6. *Type of Lesion.*—Subjects 1, 6 and 10 had a primary lesion either of the right or of the left frontal lobe. These 3 subjects (*a*) deviated widely from the average normal person in the number of errors made on some of the tests, (*b*) required assistance and special motivation to complete most of the tests attempted and (*c*) refused to complete the series of tests beyond test 6. Subject 22, in whom the left occipital lobe had been removed, also deviated widely from the average normal performance in the number of errors made on most of the tests, but her general performance was not otherwise differentiated from that of the normal group. The performance of subject 19, who had a large lesion in the left parietotemporal region, was in general superior to that of the average normal subject. Likewise, the postoperative performance of subject 25, in whom the right occipital lobe had been removed, tended to equal or exceed the average normal performance.[8]

7. *Selection of Experimental Subjects.*—By restricting our consideration in the present report to the performances of subjects with lesions of the brain who have made good, or in some instances unusually good, postoperative social adjustments, we have incidentally selected those persons who are least differentiated from normal subjects in terms of their performances on the present group of tests. The fact that marked quantitative evidence of deviation from the normal is, nevertheless, apparent in our results is therefore of particular significance.

SUMMARY

Further analysis has been made of the grouping behavior of normal subjects and of persons with lesions of the brain from the series previously reported by one of us (W. C. H.). Groups of geometric test figures having certain characteristics in common were presented by means of a special apparatus. Both qualitative and quantitative evidences of deviation from normal performance were found in some of the experimental subjects. This evidence is in line with the earlier observations of Halstead obtained on these subjects. Various factors bearing on interpretation of the present results are discussed.

University Clinics, University of Chicago.

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CALCIFICATION OF THE CEREBRAL CORTEX ASSOCIATED WITH A MENINGOTHELIOMATOUS MENINGIOMA

PATHOLOGIC STUDY, WITH COMMENT ON INCOMPLETE TYPES OF THE NEUROCUTANEOUS SYNDROME

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AND
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Intracranial calcification is not rare, and it is associated with a variety of "physiologic" and pathologic conditions. Calcification of the pineal body or of the falx cerebri occurs with such frequency that the alteration is considered physiologic by many observers. The deposition of calcareous concretions in the region of the basal ganglia has recently been reviewed extensively by Eaton, Camp and Love.[1] Their report that the calcification occurs in and about the finer cerebral blood vessels coincides with our observations in cases of a similar condition. This study, on the other hand, pertains to calcification of the brain parenchyma itself, particularly the cortex. Calcification of the cortex of the brain takes place in a variety of pathologic states, the most common being tuberous sclerosis, in which the alterations may be noted within some of the tuberosclerotic nodules. According to Yakovlev and Corwin,[2] the calcification in such lesions tends to occur not in the center of the nodule but in the periphery of the subcortical softening, facing the white matter, that is, under the cortex in the depth of the convolutions. In a closely related pathologic state, however, namely, the glial nodules of the cortex associated with Recklinghausen's disease, we have observed the calcareous concretions within the glial-sclerotic nodule itself.

The type of calcification in the cerebral cortex we are describing in this contribution has been reported and verified histologically, to our

From the Illinois Neuropsychiatric Institute; the Department of Neurology and Neurological Surgery, University of Illinois College of Medicine, and the Chicago State Hospital.

1. Eaton, L. M.; Camp, J. D., and Love, J. G.: Symmetric Cerebral Calcification, Particularly of the Basal Ganglia, Demonstrable Roentgenographically, Arch. Neurol. & Psychiat. **41**:921 (May) 1939.

2. Yakovlev, P. I., and Corwin, W.: A Roentgenographic Sign in Cases of Tuberous Sclerosis of Brain (Multiple "Brain Stones"), Arch. Neurol. & Psychiat. **42**:1030 (Dec.) 1939.

knowledge, only twice before. In both instances this alteration occurred in association with cutaneous (facial) and leptomeningeal angiomatoses. Our paper is the first in which the cortical calcification has been reported in association with a meningotheliomatous meningioma. The close genetic relationship between angioma and meningothelioma will be pointed out later, and the pleomorphic variety of incomplete or atypical forms of the neurocutaneous syndrome, of which we believe our case is an example, will be discussed.

REPORT OF A CASE

History.—Mrs. M. Z., a white woman aged 53, was admitted to the Chicago State Hospital on May 21, 1941. The onset of her illness was eighteen months before, when she began to complain of failing vision. Soon afterward, she became nervous and frightened and stayed home a great deal. She was taken to an ophthalmologist, who reported that her right eye was totally blind and that vision in her left eye was reduced to counting fingers at a distance of 8 feet (245 cm.). The left pupil reacted sluggishly to light, and the right pupil did not react at all. Examination of the optic fundi revealed bilateral advanced primary optic nerve atrophy. The Wassermann reaction of the blood was negative, and roentgenograms of the skull showed no abnormalities. The pathogenesis of the primary optic nerve atrophy could not be determined. A short time afterward she was in an automobile accident, in which she sustained minor bruises. After this incident her nervousness increased and she became confused and agitated. She imagined she was not at home and demanded that she be taken home. She imagined seeing dogs and little children, to whom she talked. She became very jealous of her husband, pulled his hair, scratched his face and called him vile names. As her mental condition became progressively worse, she was admitted to the Cook County Psychopathic Hospital on May 18, 1941 and shortly thereafter was transferred to the Chicago State Hospital, with a diagnosis of presenile dementia.

Physical Examination.—Inspection revealed her to be well nourished. The heart was enlarged to the left, and a soft systolic murmur was heard at the apex. The blood pressure was 150 systolic and 90 diastolic. The olfactory sense was not tested. With the exception of advanced bilateral primary optic nerve atrophy, no abnormalities were found in the neurologic examination.

Laboratory Data.—The blood count revealed 4,500,000 red cells per cubic millimeter, 14.5 Gm. of hemoglobin per hundred cubic centimeters and 5,200 white cells per cubic millimeter. The Kahn reaction of the blood was negative. The Pandy reaction of the cerebrospinal fluid was faintly positive; the Lange colloidal gold curve was 0000000000. The sugar content of the cerebrospinal fluid was 74 mg. per hundred cubic centimeters.

Mental Examination.—After admission to the hospital the patient was quiet and cooperative. She appeared apathetic and was grossly disoriented, and there was no play of emotions on her face as she spoke. When asked about her vision she said, "I can't be blind; I see everything." On questioning, however, it was apparent that she could not count fingers at a distance of 3 feet (90 cm.). The first clinical impression was that of organic disease of the brain, undetermined of type.

On June 9 an electroencephalographic study was made by Dr. Chester W. Darrow, of the psychophysiologic laboratory of the Illinois Institute for Juvenile

Research. He reported that the patient was quiet and cooperative throughout the examination. The record showed a large amount of 2 to 3 per second waves of large potential arising from the frontal and the motor regions. He expressed the opinion that the tracings from all areas were suggestive of degenerative changes in the brain. On June 11 pneumoencephalographic examination revealed moderate diffuse internal hydrocephalus of the lateral and third ventricles.

Clinical Diagnosis.—In view of the clinical history and course, the degenerative changes evidenced by the brain waves and the moderate and symmetric internal hydrocephalus, the majority opinion of the staff members was that the patient was suffering from a form of presenile dementia, probably Alzheimer's disease. The primary optic nerve atrophy, however, remained unexplained.

Course.—The patient's mental condition continued to be poor; bronchopneumonia developed, and she died on Nov. 3, 1941.

Anatomic Diagnosis.—The diagnosis was meningotheliomatous meningioma arising from the leptomeninx in the vicinity of the olfactory tracts; Alzheimer's disease; focal and confluent bronchopneumonia, and calcification of the cerebral cortex of the convolutions adjacent to the meningioma.

Gross Pathologic Observations.—The brain was removed and hardened in a dilute concentration of solution of formaldehyde U. S. P. (1:10). The leptomeninges were everywhere thin and transparent. The blood vessels at the base of the brain contained single sclerotic plaques. On the orbital surface of the frontal lobe, just in front of the hypophysis, was a round, disk-shaped tumor 4 cm. in thickness. This tumor compressed both olfactory tracts, both optic nerves and the optic chiasm. It was firmly adherent to the roof of both orbits, into which it had grown. After fixation, the brain was cut in a midsagittal plane. That portion of the tumor which bordered on the parenchyma of the brain was soft and grayish white and measured up to 10 mm. in thickness. This soft tissue merged rather sharply into the sclerotic portion of the tumor that had grown into the roof of both orbits. On section of the brain, the lateral and third ventricles were observed to be moderately dilated. The cortex and the basal ganglia were dark gray brown. When the orbital gyri were sectioned, the knife encountered calcific material.

Microscopic Pathologic Observations.—Tumor: The soft portion of the tumor showed the typical histologic picture of a meningotheliomatous meningioma (fig. 1). It was composed of alveoli of mesothelial cells of uniform appearance. The alveoli were separated by interlacing bundles of collagenous connective tissue, which stained deep red with Van Gieson's method. This portion merged rather sharply into the sclerotic portion, in which islands of tumor tissue were separated by trabeculae of bone (fig. 2).

Brain: The leptomeninges were thin and free from cellular infiltrations. The cytoarchitecture was, on the whole, well preserved. Here and there throughout the cortex, clear areas devoid of cellular elements were seen, and in many areas the ganglion cells appeared pale and shrunken. In the deeper layers of the cortex a moderate degree of satellitosis was observed. The calcific material described in the gross specimen took the dyes rather deeply. The largest concretions were seen in the center of the affected area (fig. 3). Here the concretions were round and the internal lamination was distinct. In adjacent areas, structures identical with the corpora arenacea, or the so-called brain sand granules, commonly seen in the pineal body were observed. In the periphery of the affected zone, spherical, centrally laminated concretions no larger than the nuclei of ganglion cells were

arranged in nests. The concretions which were most recently precipitated were not laminated but were rather amorphous and granular. Many of the concretions had fallen out, leaving clear areas. There was no increase in glia about the

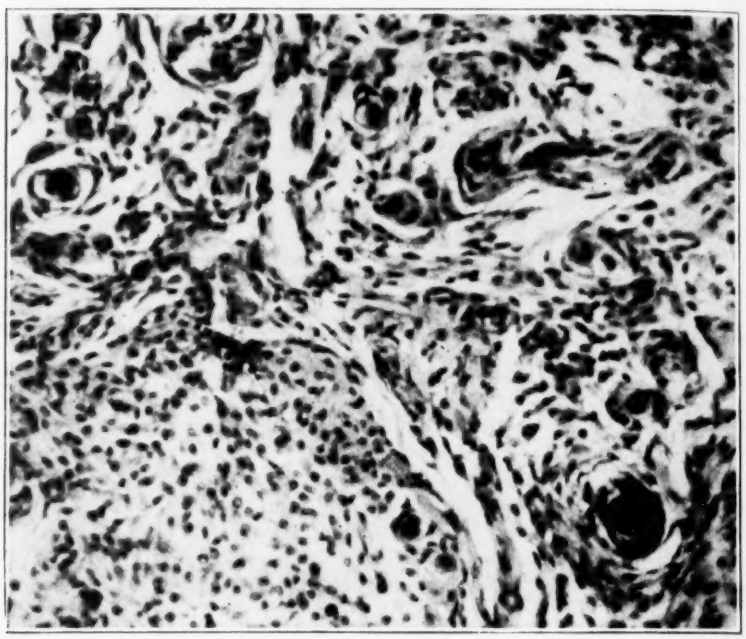

Fig. 1.—Low power photomicrograph of a portion of the tumor, showing the whorls characteristic of a meningotheliomatous meningioma. Iron hematoxylin stain.

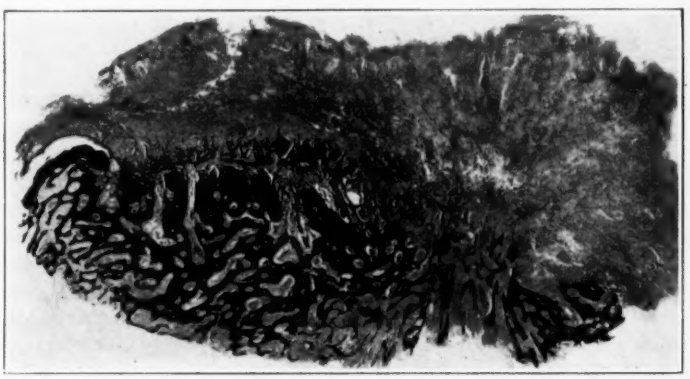

Fig. 2.—Low power photomicrograph of the meningioma. The deeply stained tissue in the lower part of the tumor is trabeculae of bone. Van Gieson stain.

concretions. In Bielschowsky preparations the concretions were surrounded by clear areas devoid of neurofibrils (fig. 4 *B*). More striking, however, were the large numbers of senile plaques scattered throughout all portions of the cortex

of the brain. Ganglion cells showing the condensed and spiral neurofibrillary apparatus characteristic of Alzheimer's disease were seen in large numbers in all fields (fig. 4 *A*).

CLINICAL CONSIDERATIONS

The clinical diagnosis of Alzheimer's disease, corroborated by electroencephalographic evidence of degeneration of the nervous system and pneumoencephalographic evidence of atrophy of the cortex of the brain, was verified by the microscopic examination. The bilateral primary optic nerve atrophy, however, which resulted from the pressure of the meningioma on the optic nerves and the optic chiasm, was a disturbing clinical observation. A stereoscopic examination of the lateral roentgenograms of the skull taken at the time the encephalogram was obtained showed a faintly outlined but rather distinct shadow just above the orbits in the

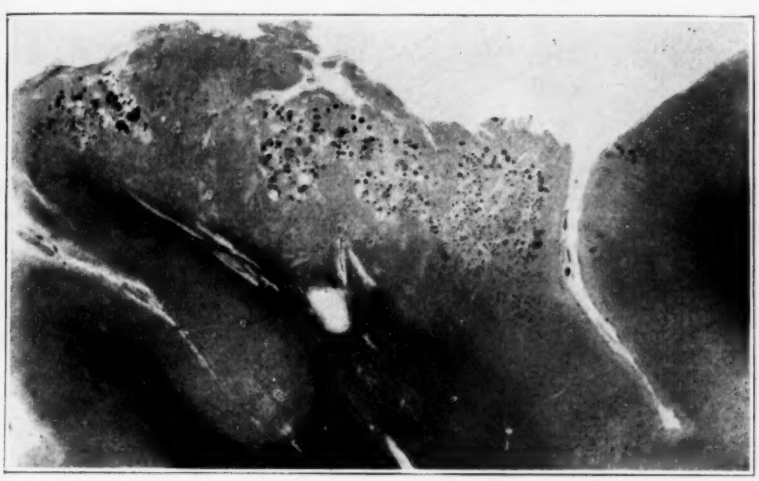

Fig. 3.—Low power photomicrograph through the orbital gyrus, showing the intracortical concretions. Weil stain.

region where the sclerotic portion of the meningioma was seen. The calcification in the brain substance itself could not be detected in the roentgenograms. It is unfortunate that the olfactory sense was not examined, since anosmia coupled with primary optic nerve atrophy might have suggested the possibility of a basofrontal lesion just in front of the optic chiasm.

PATHOLOGIC CONSIDERATIONS

From the histologic study of the case reported it is evident that one is dealing with a meningotheliomatous meningioma associated with intracortical calcifications in the adjacent convolutions. Both conditions were present in a brain showing histologic evidence of Alzheimer's disease.

We believe that it will be the consensus that the Alzheimer disease was not pathogenetically related to the other two states. Many investigators may contend that the meningothelioma, too, was wholly unrelated to the

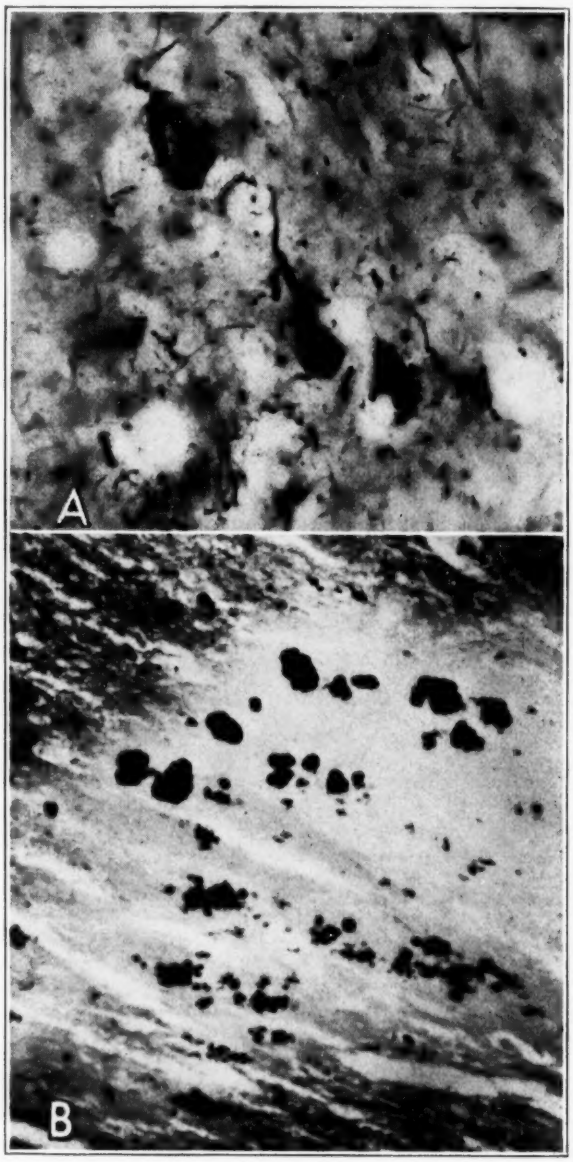

Fig. 4.—*A*, high power photomicrograph of a section through the cerebral cortex, showing the Alzheimer changes in the ganglion cells.

B, low power photomicrograph of a section through the cortex, showing the concretions surrounded by clear areas devoid of neurites. Bielschowsky stain.

intracortical calcifications, but we shall attempt to show that the coexistence of the latter two pathologic states was not accidental.

The medical literature is replete with instances in which cutaneous anomalies have been associated with neurologic disorders. The two outstanding disorders belonging to this group are Recklinghausen's disease and tuberous sclerosis. To them is added von Hippel-Lindau disease, in which the external evidence of disorder is present not in the skin but in the eye. Of these three disorders atypical (incomplete, central or latent) varieties occur in which external evidences are lacking despite the involvement of the nervous system.

In addition to these three major types of the so-called neurocutaneous syndrome, many minor ones occur, among them being Sturge-Weber disease. The pathologic syndrome we are describing is closely related to the latter disorder.

The combination of a vascular nevus in the trigeminal region with telangiectasis of the pia mater and angiomatosis of the brain was first described clinically by Sturge [3] in 1879. Kalischer,[4] in 1897, described the anatomic changes in a case of this condition. Weber,[5] first in 1922 and later in 1929, described the roentgenographic alterations in the brain of a patient presenting a vascular nevus of the face with contralateral hemiplegia. In his 1929 publication, the sinuous calcified shadow corresponding to the surface of the brain was clearly seen. Dimitri,[6] in 1923, published the report of a case in which an angioma of the brain produced a distinct shadow in the roentgenogram, and Marque,[7] in 1927, described 2 cases with similar roentgenographic changes. Because of the presence of the vascular nevus on the face, the calcifications seen in the roentgenograms were interpreted as calcified angiomas.

Krabbe,[8] in 1934, published the anatomic observations in the case of a white youth aged 19 years who since birth had had a large vascular

3. Sturge, A.: A Case of Partial Epilepsy, Apparently Due to a Lesion of One of the Vaso-Motor Centers of the Brain, Tr. Clin. Soc., London **12**:162, 1879.

4. Kalischer, S.: Demonstration des Gehirns eines Kindes mit Telangiectasie der linksseitigen Gesichtskopehaut und Hirnoberfläche, Berl. klin. Wchnschr. **33**: 1059, 1897.

5. Weber, F. P.: Right-Sided Hemi-Hypotrophy Resulting from Right-Sided Congenital Spastic Hemiplegia, with a Morbid Condition of the Left Side of the Brain Revealed by Radiograms, J. Neurol. & Psychopath. **3**:134, 1922; A Note on the Association of Extensive Hemangiomatous Naevus of the Skin with Cerebral (Meningeal) Haemangioma, Especially Cases of Facial Vascular Naevus with Contralateral Hemiplegia, Proc. Roy. Soc. Med. (Sect. Neurol.) **22**:431, 1929.

6. Dimitri, J.: Rev. Asoc. méd. argent. **36**:1029, 1923.

7. Marque, A.: Consideraciones sobre angiomas en la infancia, Rev. oto-neuro-oftal. **1**:202, 1927; cited by Krabbe.[8]

8. Krabbe, K. H.: Facial and Meningeal Angiomatosis Associated with Calcifications of the Brain Cortex, Arch. Neurol. & Psychiat. **32**:737 (Oct.) 1934.

nevus over the right side of his face. Roentgenograms of the skull showed an irregular shadow in the right occipital lobe corresponding to the cerebral gyri, with darker lines corresponding to the sulci. Some of the darker lines had double contours. The patient had been subject to epileptiform seizures for several years, and death followed several attacks. Histologic examination of the brain showed that the shadow seen in the roentgenogram was due to calcification of the outer layers of the cortex, and not of the pia mater or the blood vessels in its vicinity. The calcification consisted of small granules of lime salts localized in the second and third layers of the cortex. The pia mater over the calcified area was abundantly vascularized, but no true angioma was seen.

Intracortical calcification, as seen in our case and in the case reported by Krabbe, was seemingly first reported by Volland [9] in 1913, whose case was clinically and pathologically similar to Krabbe's. Volland's patient, a boy, had suffered from epileptiform attacks, and his mental development had been slow. There was a vascular nevus on the left side of his face, and he had contralateral hemiplegia. Autopsy revealed that the left cerebral hemisphere was smaller than the right. The pia mater over the left side of the brain, particularly in the region of the frontal bone over the base of the third frontal convolution, over the tip of the temporal lobe and over the left cuneus, was greatly thickened and was rich in blood vessels. Microscopically, the leptomeninges were seen to be the seat of angiomatous formations. In the sclerotic areas of the brain, particularly in the left occipital lobe, but also to a less degree in the left frontal lobe and in the cornu ammonis, the cortex, and to a lesser degree the subcortical white substance, was the seat of many calcareous concretions.

The calcification in Volland's case was much more extensive than in either Krabbe's case or the one described in this report. Volland's case and that of Krabbe were similar in that the intracerebral calcifications were associated with leptomeningeal angiomatoses and cutaneous vascular nevi. Our case differed from theirs in two ways—first, no cutaneous lesion was present, and, second, instead of an angiomatous meningioma of the leptomeninx, a meningotheliomatous meningioma was present. On analysis, one sees that these differences are minor and that our case belongs to the same group as theirs. The absence of cutaneous manifestations in any case of the neurocutaneous syndrome (Recklinghausen's disease or tuberous sclerosis) is not rare, and in such instances the condition is usually designated as incomplete, central, abortive or latent. More common than the abortive peripheral type is

9. Volland: Ueber zwei Fälle von zerebralem Angiom nebst Bermerkungen über Hirnangiome, Ztschr. f. d. Erforsch. u. Behandl. d. jugendl. Schwachsinns **6**:130, 1913.

the abortive or incomplete central type, in which cutaneous manifestations are present without changes in the meninges or the central nervous system. Examples of this type are the vascular nevi of the face unassociated with meningeal or cerebral alterations. In some instances a mixed type of the neurocutaneous syndrome occurs, as in the case reported by Grieg,[10] in which adenoma sebaceum of the face (Pringle's disease), which is usually observed in association with tuberous sclerosis, accompanied a meningeal nevus.

The differences between an angiomatous meningioma, such as the tumor in the cases of Volland and Krabbe and a meningotheliomatous meningioma, such as the tumor in our case, are minor. The primitive leptomeninx, regardless of the fact that it may originate from the neural crest and is, therefore, ectodermal in origin, according to the observations of Harvey and Burr,[11] is histopathologically mesenchymal in character. The early mesenchyma may be considered to be the parent organ of two types of tissue—the nutritive (blood vessels) and the supportive. The angiomatous meningioma is basically a growth of the nutritive (vascular) component of the primitive leptomeninx, and the meningotheliomatous meningioma is essentially the most common type of growth arising from the supportive component of the primitive leptomeninx. According to Bailey and Bucy,[12] at least nine varieties of meningeal tumors have been differentiated, and it is our belief that in the future varieties other than angioma and meningothelioma will be observed in association with cerebral calcification.

Terminology has always been a difficult part of clinical medicine, especially when one is dealing with incomplete, poorly recognized or little known diseases.

Krabbe,[8] in his contribution on facial and meningeal angiomatoses associated with calcification of the cerebral cortex, closed with the sentence, "If this disease, forming an entity, should deserve a name, it might well be Parkes Weber-Dimitri's disease." Weber [5] (August 1922) and Dimitri [6] (1923) were the first, it will be recalled, to record the characteristic roentgenographic changes, which Krabbe showed were due to intracerebral calcification rather than to calcified blood vessels. Since Krabbe [8] (1934) was the first to demonstrate that the sinuous shadows seen in the roentgenogram were indicative of calcification in the cortex

10. Grieg, D. M.: A Case of Meningeal Naevus Associated with Adenoma Sebaceum, Edinburgh M. J. **28**:105, 1922.

11. Harvey, S. C., and Burr, H. S.: The Development of the Meninges, Arch. Neurol. & Psychiat. **15**:545 (May) 1926. Harvey, S. C.; Burr, H. S., and Van Campenhout, E.: Development of Meninges, ibid. **29**:683 (April) 1933.

12. Bailey, P., and Bucy, P. C.: The Origin and Nature of Meningeal Tumors, Am. J. Cancer **15**:15, 1931.

of the brain, many authors (Moniz and Lima [13]) have alluded to the disorder as Krabbe's disease. It was Volland [9] (1913), however, who first showed that the calcifications noted in the brain of a boy with a facial vascular nevus were in the brain substance itself and not in the blood vessels. Since Sturge [3] was apparently the first to describe the neurocutaneous syndrome clinically, the association of vascular nevi of the face, particularly in the region of distribution of the trigeminal nerve, with the characteristic roentgenographic shadows, first described by Weber,[5] is now termed the Sturge-Weber syndrome.

The association of epilepsy with progressive facial hemiatrophy has been noted by many observers. Merritt, Faber and Bruch [14] called attention to the presence of sinuous shadows in the roentgenograms of the skull of patients with progressive facial hemiatrophy. These shadows closely conform to what has been described in the past as indicative of calcified angioma (Weber and Dimitri), but which Krabbe showed to be intracortical, nonvascular calcifications. The cause of progressive facial hemiatrophy is indefinite. According to some authors, the disorder is the manifestation of a form of scleroderma. A striking histopathologic alteration in cases of scleroderma is the diffuse increase in the connective tissue. This growth of connective tissue—rich in collagen—constricts the nutrient blood vessels, and atrophy of the affected tissues may result. It is important to remember that hemangiomas, too, undergo sclerosis. This process, which is much more pronounced in some cases than in others, is also characterized by an overgrowth of collagenous connective tissue, which finally obliterates the blood vessels. Thus, in cases both of hemangioma (to which the vascular nevus belongs) and of progressive facial hemiatrophy, a diffuse overgrowth of connective tissue may occur. Both conditions, too, may be associated with epilepsy and Dimitri-Weber cerebral calcifications. In many instances of vascular nevi of the face the angiomatous process involves the subcutaneous tissue, the muscles, the fasciae and the skull itself. Similarly, in cases of progressive facial hemiatrophy the atrophic-sclerotic process may involve the skin, the subcutaneous fat, the connective tissue, the muscles and the bones. The association of pigmentary with vascular nevi is well known, and the occurrence of pigmentary nevi with progressive facial hemiatrophy has also been observed.

Geyelin and Penfield,[15] reported the clinical and roentgenographic observations in cases of a "peculiar type of epilepsy" that appeared in

13. Moniz, E., and Lima, A.: Pseudo-angiomes calcifies du cerveau, angiome de la face et calcifications corticales du cerveau (maladie de Knud H. Krabbe), Rev. neurol. **63**:743, 1935.

14. Merritt, K. K.; Faber, H. K., and Bruch, H.: Progressive Facial Hemiatrophy, J. Pediat. **10**:374, 1937.

15. Geyelin, H. R., and Penfield, W.: Cerebral Calcification Epilepsy, Arch. Neurol. & Psychiat. **21**:1020 (May) 1929.

one family, including the father and all 4 children. Roentgenograms in 4 of the cases showed distinct calcified areas in the brain substance. In many instances the shadows appeared circular or tubular, with furrows that seemed to follow the fissures of the brain. Many of these shadows were identical with those described by Weber and Dimitri. In 1 instance craniotomy was performed, which revealed the calcified areas to be harder than normal and the overlying leptomeninx less vascular than usual. Microscopic examination revealed that the calcification "began in the deeper layers of the gray matter and extended into the white matter." In the center of the calcified zone were loosely arranged fibrous neuroglia cells and many scattered calcified granules, the size of which varied from less than the diameter of the nucleus of a nerve cell to the size of a Betz cell. "The small capillaries stood out and seemed to be numerous but were frequently converted into calcified tubes."

According to Geyelin and Penfield, the primary change in their case was a local vascular one. Obliteration had taken place in the small vessels, which resulted in local destruction of cerebral tissue, and the calcification was secondary to this local destruction. They stated that the process might be called "obliterating endarteritis of the cerebral hemispheres."

It is difficult to decide whether the calcification described by Geyelin and Penfield is of the Weber-Dimitri type. In the cases of Volland and Krabbe and in our case the blood vessels were not calcified. In the case of Geyelin and Penfield, however, the calcification was not restricted to the blood vessels but was loose in the parenchyma as well.

We do not believe that it is germane to this contribution to discuss the chemical nature of the concretions which have been so loosely referred to as calcium. Suffice it to say that debate has arisen as to the exact chemical nature of the deposits.

It should be emphasized that angiomas of the brain do undergo calcification, but the roentgenographic changes are not similar to those seen with the type of calcification described in this report.

SUMMARY AND CONCLUSIONS

The clinical and pathologic features of a case of Alzheimer's disease complicated by the presence of a large meningioma of the olfactory groove are presented.

The suggestion is made that the association of calcification of the cerebral cortex with the meningothelioma is part of a pathologic complex and not a mere coincidence.

The association of the Dimitri-Weber calcifications in the brain with pathologic conditions other than vascular nevi in the region of distribution of the trigeminal nerve (Sturge-Weber syndrome) is reviewed.

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NEUROGENIC HYPERTHERMIA AND ITS TREATMENT WITH SOLUBLE PENTOBARBITAL IN THE MONKEY

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Within recent years an increasing number of papers have appeared on neurogenic hyperthemia, a severe and occasionally fatal elevation of body temperature which sometimes results from acute injury to the brain, especially if the hypothalamic region has been involved (Cushing,[1] Gagel,[2] Alpers,[3] Dott,[4] Erickson,[5] Davison[6] and Zimmerman[7]). This acute hyperthermia, which Cushing[1] characterized as a bête noire

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† Dr. Ranson died Aug. 30, 1942.

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1. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C Thomas, Publisher, 1932.

2. Gagel, O.: Symptomatologie der Erkrankungen des Hypothalamus, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 5, pp. 482-522.

3. Alpers, B. J.: Hyperthermia Due to Lesions in the Hypothalamus, Arch. Neurol. & Psychiat. **35**:30-42 (Jan.) 1936.

4. Dott, N. M.: Surgical Aspects of the Hypothalamus, in Clark, W. E. LeG.; Beattie, J.; Riddoch, G., and Dott, N. M.: The Hypothalamus, London, Oliver & Boyd, 1938, pp. 131-185.

5. Erickson, T. C.: Neurogenic Hyperthermia (A Clinical Syndrome and Its Treatment), Brain **62**:172-190, 1939.

6. Davison, C.: Disturbances of Temperature Regulation in Man, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:774-823, 1940.

7. Zimmerman, H. M.: Temperature Disturbances and the Hypothalamus, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:824-840, 1940.

of the neurosurgeon, has been ascribed to a dysfunction of the hypothalamic temperature-regulating mechanism, and a variety of antipyretic agents have been utilized in attempts to control it, but without success. In 1938, Dott [4] wrote:

> We know of no pharmacological substance which will effectively lower the raised temperature in cerebrogenic hyperthermia. Artificial cooling is our only effective treatment.

It appeared that if acute hyperthermia could be produced with some regularity by hypothalamic injury in experimental animals, an opportunity would be afforded for a study of the treatment of this disorder. In 1935 Ranson and Ingram [8] reported cases of postoperative elevation of body temperature following injury to the anterior portion of the hypothalamus in a series of monkeys operated on under anesthesia induced with soluble pentobarbital U. S. P. (pentobarbital sodium). It was noted that the hyperthermia did not commence until some hours after operation, when the animals had recovered from the anesthetic, and this suggested that pentobarbital might be an effective therapeutic agent for hyperthermia. By 1938 investigation of the temperature-regulating mechanisms in the hypothalamus had progressed to the extent that it was possible to report the results of a series of controlled experiments in which lesions in the anterior portion of the hypothalamus of cats, operated on under ether, resulted in postoperative hyperthermia, which was reduced by the injection of soluble pentobarbital (Ranson and Clark [9]). It was stated [9]:

> The possibility that this drug [nembutal] might be useful in combating neurogenic hyperthermia in man should receive the consideration of neurosurgeons.

The clinical importance of the observation appeared to warrant further study, and the following report is concerned with the results of additional investigation of experimental hyperthermia and its treatment with pentobarbital in a series of monkeys.

METHOD

With use of the Horsley-Clarke technic (Ranson [10]), and with full aseptic precautions, bilateral electrolytic lesions were placed in the hypothalamic region of monkeys under ether anesthesia. After operation, the animals were confined in a hammock in a room at or a little above 80 F. A continuous record of their rectal temperature was obtained with a Leeds and Northrup micromax, and they were observed at frequent intervals over a period of twenty-four to forty-

8. Ranson, S. W., and Ingram, W. R.: Hypothalamus and Regulation of Body Temperature, Proc. Soc. Exper. Biol. & Med. **32**:1439-1441, 1935.

9. Ranson, S. W., and Clark, G.: Neurogenic Fever Reduced by Nembutal, Proc. Soc. Exper. Biol. & Med. **39**:453-455, 1938.

10. Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. **38**:534-543, 1934.

eight hours. In each case the body temperature fell after the induction of anesthesia, and while the animal was being prepared for operation. During the operation external heat was applied, and in many instances the temperature rose. The anesthetic and the external heat were discontinued at the end of the operation, but the block marked *ANES* in the temperature charts includes the time required for recovery. The body temperature before and during the operation was influenced by the anesthetic and by the application of external heat, and only those changes which occurred after the termination of the operation can be regarded as significant.

Tests of temperature regulation in the chronic state were made by placing the animal in an ice box at 32 F. or by confining it in a hotbox at 122 F. The monkey's head and hands protruded from the hotbox so that observations could be made on sweating and respiration. Preoperative tests made on each animal served for comparison. At autopsy the location and extent of the lesions were verified by microscopic examination of serial sections through the hypothalamic region of the brain.

TEMPERATURE REGULATION IN THE ACUTE STATE

Control Experiments.—The disorders in temperature regulation to be described can best be appreciated against a background furnished by the acute postoperative course of 3 monkeys subjected to the same anesthetic and operative procedure, but in which the lesions were not in a position to affect the hypothalamic temperature-regulating mechanisms. The location of the lesions in these control animals was anterior (monkey 1, fig. 1), dorsal (monkey 2, fig. 2) and lateral (monkey 3, fig. 3) respectively to the preoptic region and the anterior portion of the hypothalamus. When placed in a room at 80 F. or above after operation, the animals either maintained their body temperature within the normal range of 100 to 102 F. from the start (monkey 3, fig. 3) or did so after a transient fall to 97.6 F. (monkey 1, fig. 1) or 98.6 F. (monkey 2, fig. 2). They subsequently exhibited normal temperature regulation throughout the period of survival.

Fatal Hyperthermia.—In striking contrast to the controls, 9 other monkeys, in which symmetric bilateral lesions were produced within the preoptic region or the anterior portion of the hypothalamus, exhibited severe, acute postoperative hyperthermia. In 2 animals of this group the hyperthermia was allowed to proceed without treatment, and the observations on these animals may first be presented.

In monkey 4 the large bilateral lesion of the preoptic region shown in figure 4*B* was produced. The postoperative course is illustrated in figure 4*A*. The animal's temperature was maintained between 101 and 101.5 F. during the operation. One-half hour after operation, when the animal appeared to have fully awakened from the anesthesia, its temperature began to rise in almost a linear fashion and reached a peak of 109.1 F. five hours after operation. The animal then became comatose; its temperature fell gradually to 108 F., then rapidly to 106.5 F., and it died. The heart rate, which remained between 200 and 230 per

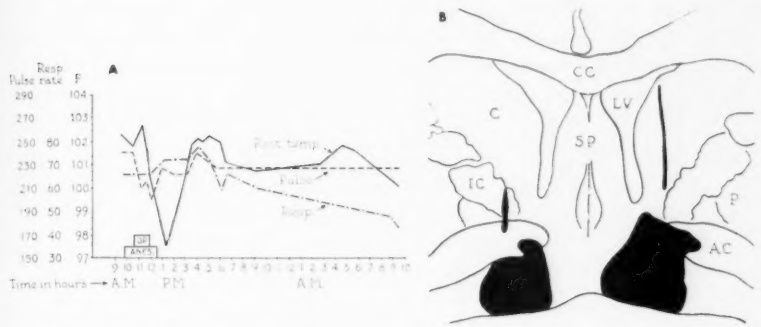

Fig. 1 (monkey 1).—*A*, temperature chart; *B*, lesions in the brain.

In this figure and in the accompanying figures, the following abbreviations are used: *AC*, anterior commissure; *BP*, basis pedunculi; *C*, caudate nucleus; *CC*, corpus callosum; *F*, fornix; *GP*, globus pallidus; *IC*, internal capsule; *LV*, lateral ventricle; *MB*, mamillary body; *MI*, massa intermedia; *NR*, red nucleus; *OC*, optic chiasm; *OT*, optic tract; *P*, putamen; *SP*, septum pellucidum; *VA*, nucleus ventralis anterior, and *III*, third ventricle.

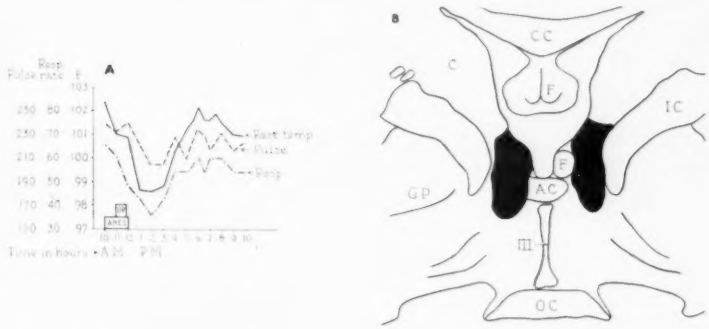

Fig. 2 (monkey 2).—*A*, temperature chart; *B*, lesions in the brain.

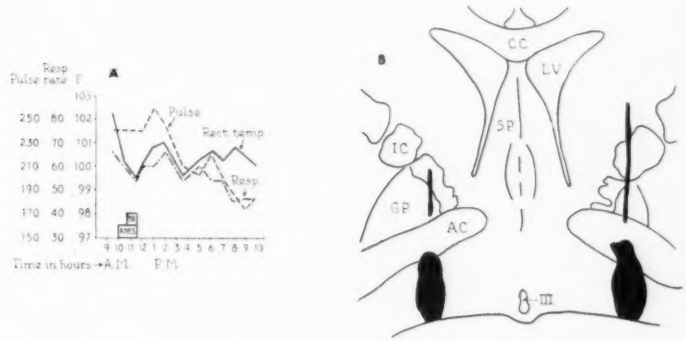

Fig. 3 (monkey 3).—*A*, temperature chart; *B*, lesions in the brain.

minute during the course of the operation and immediately thereafter, became elevated with the rise in temperature and reached a peak of 360 per minute just before death. The respiratory rate, which was between 50 and 65 per minute during the operative period, rose only slightly during the period of hyperthermia, to between 65 and 80 per minute. With a rectal temperature of 108 F. the animal exhibited some shivering, and at 109 F. piloerection occurred. Though the trunk was warm and some rubor of the chest was observed, the extremities remained cold, and at no time during the hyperthermia did the animal sweat.

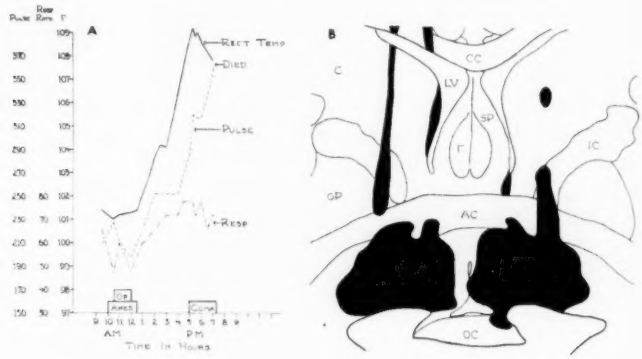

Fig. 4 (monkey 4).—*A*, temperature chart; *B*, lesions in the brain.

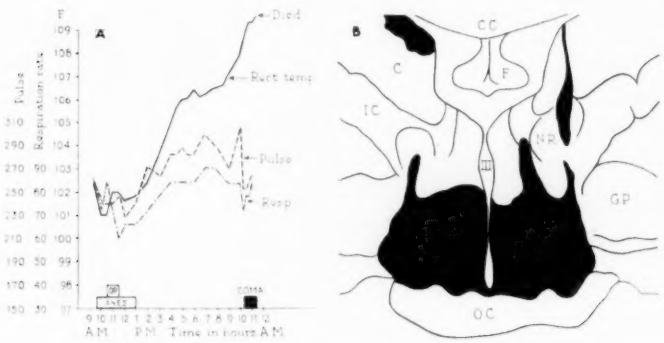

Fig. 5 (monkey 5).—*A*, temperature chart; *B*, lesions in the brain.

In monkey 5 the large bilateral lesion of the preoptic region and the anterior part of the hypothalamus seen in figure 5 *B* was produced. The postoperative course is charted in figure 5 *A*. The animal's temperature was maintained between 101 and 102 F. during the operation. One and one-half hours after operation, when the monkey appeared fully awake, its temperature began to rise and four hours later had reached 106 F. During the next three hours the temperature did not vary greatly, but thereafter rose rapidly and reached 109.1 F. eleven hours after operation. At this time the animal became comatose, but remained alive another forty-five minutes, the temperature at death being 109.5 F. The heart rate, between 230 and 250 per minute during and shortly after operation, showed some tendency to increase with the rise in temperature, the highest rate being 300 per minute. A slight increase in respiratory rate occurred. The

animal exhibited some piloerection and a little shivering during the latter part of the period of hyperthermia. Though the trunk felt very hot, the extremities remained cold, and the animal did not sweat.

The cases of these 2 monkeys illustrate severe, acute hyperthermia following appropriately situated injury to the temperature-regulating mechanism in the preoptic region and the anterior part of the hypothalamus. The rise in body temperature commenced one-half to one and one-half hours after operation, on recovery from the ether anesthesia, and proceeded to a peak above 109 F., when coma supervened and the animals died, seven and twelve hours after operation.

Reduction of Severe Hyperthermia with Soluble Pentobarbital.—In each of 7 other monkeys of the group with severe, acute hyperthermia, soluble pentobarbital proved an effective agent in reducing the hyperthermia, and with its aid 6 of the animals were brought through their

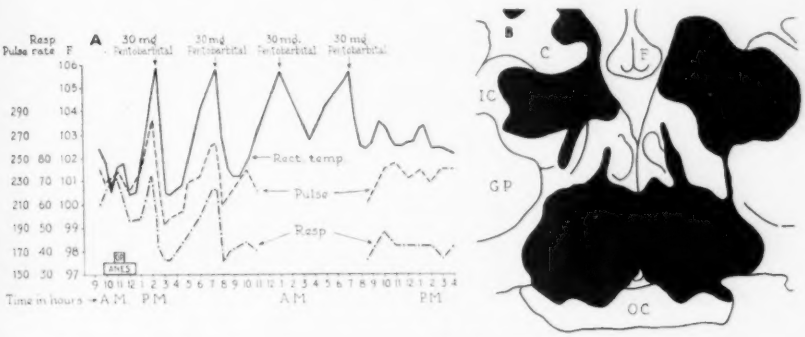

Fig. 6 (monkey 6).—*A*, temperature chart; *B*, lesions in the brain.

turbulent postoperative periods to survival. In administering pentobarbital in these cases, it was first essential to allow the hyperthermia to proceed to a point at which it became clear that the rise in temperature was severe, and if left unattended would probably proceed to death. Second, it was necessary to administer the drug before the hyperthermia had developed to the point at which the animal could no longer recover. In the single case of fatality in this group, pentobarbital was not given until the body temperature had reached 107 F.; in the remaining cases it was administered when the body temperature had reached 106 F. and as often thereafter as seemed desirable. The cases of each of the animals may be presented.

Monkey 6 suffered a large lesion of the preoptic region and the anterior portion of the hypothalamus, and anemic softening extended the destruction into the adjacent basal ganglia and the internal capsule on each side (fig. 6 *B*). Two and one-half hours after operation (fig. 6 *A*) its temperature had risen to 106 F., and 30 mg. of soluble pentobarbital was given intravenously. The temperature fell to 100.4 F., but eight hours after operation it had returned to 105.7 F. Thirty milligrams of soluble pentobarbital was again given, and the temperature fell to

101.2 F. Thirteen hours after operation the temperature had risen once more to 105.7 F., and again 30 mg. of soluble pentobarbital was given, the temperature falling to 102.8 F. A fourth peak of 105.6 F. was reached nineteen hours after operation, and a fourth injection of 30 mg. of soluble pentobarbital reduced the temperature to 102.4 F. The hyperthermia then appeared to have been definitely broken, though temperatures between 103 and 104 F. were subsequently encountered as late as the afternoon of the second postoperative day. On the third and fourth postoperative days the animal's temperature varied within the normal range, between 100.4 and 102.2 F. Because of its poor condition, which was attributed to the extensive lesion, the animal was killed on the fourth postoperative day.

In monkey 7 a small bilateral lesion of the preoptic region and the anterior portion of the hypothalamus was produced (fig. 7 *B*). As seen in figure 7 *A*, two hours after operation its temperature had risen to 106 F., and 40 mg. of soluble pentobarbital was given intravenously. The temperature fell to 103 F., but nine hours after operation it had again risen to 106.6 F. Forty milligrams of soluble

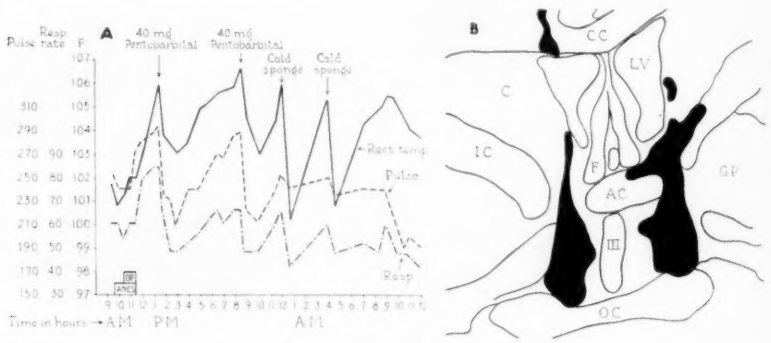

Fig. 7 (monkey 7).—*A*, temperature chart; *B*, lesions in the brain.

pentobarbital was again administered, and the temperature once more fell to 103 F. Twelve and sixteen hours after operation the animal's temperature had reached the third and fourth peaks, respectively, between 105 and 106 F., but on these occasions, with the back of the hyperthermia broken by pentobarbital, cold sponging proved effective in reducing the temperature. A fifth elevation, to 105.5 F., was encountered twenty-one hours after operation, but the temperature gradually fell without treatment, and on the second postoperative day the reading of 102.6 F. was almost within the normal range. The animal survived without further incident, and the results of subsequent tests of its temperature regulation in the chronic state will be presented in a later section.

In monkey 8 a small bilateral lesion of the preoptic region was produced (fig. 8 *B*). Two hours after operation (fig. 8 *A*) its temperature had risen to 106 F., and 40 mg. of soluble pentobarbital was given intravenously. The temperature fell to 102 F., but six hours after operation it had again risen to 106 F. Then 52 mg. of soluble pentobarbital was administered intraperitoneally, and a decided drop in temperature, to 98.2 F., resulted. Thirteen hours after operation the temperature had again risen to 105 F., but from this level it fell without further treatment to between 103 and 104 F. On the second postoperative day the hyperthermia was still present, and the animal was found in the morning with a temperature of 105.8 F. This was reduced by cold packing to

102.2 F., and the subsequent course of the animal was uneventful. Tests of its temperature regulation in the chronic state will be given later.

In monkey 9 a small preoptic lesion (fig. 9 *B*) resulted three hours after operation in a temperature of 106.1 (fig. 9 *A*). Forty milligrams of pentobarbital was given intravenously, and the temperature fell to 101.4 F. It subsequently rose to 105.8 F., but waned gradually and varied between 104 and 105 F., without further treatment, for about twenty-four hours after operation. The further course of the animal was uneventful, and the results of tests of temperature regulation in the chronic state will be given later.

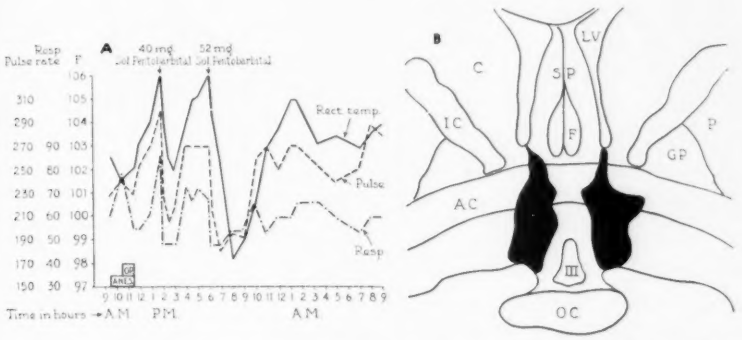

Fig. 8 (monkey 8).—*A*, temperature chart; *B*, lesions in the brain.

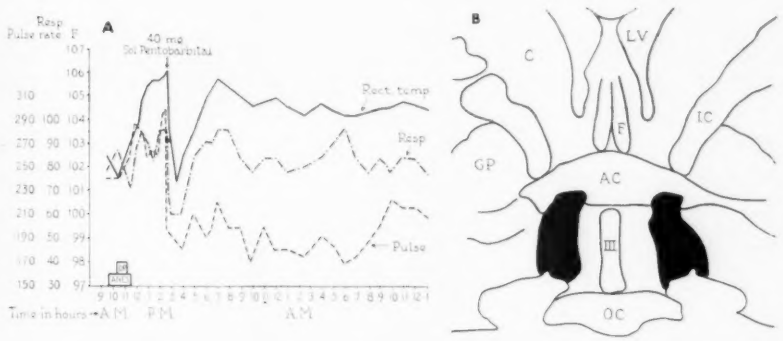

Fig. 9 (monkey 9).—*A*, temperature chart; *B*, lesions in the brain.

Monkey 10 suffered a lesion of the preoptic region and the anterior portion of the hypothalamus (fig. 10 *B*). The hyperthermia was more gradual than usual (fig. 10 *A*) but reached 106.1 F. seven hours after operation. Then 35 mg. of soluble pentobarbital was given intravenously, and the temperature fell to 103.6 F. Subsequent administration of 35 mg. of soluble pentobarbital subcutaneously had little further effect, but with cold packing eleven hours after operation the temperature was reduced to 102 F. and did not again rise greatly. The chronic course of the animal will be discussed later.

In monkey 11 a large lesion of the anterior part of the hypothalamus was produced (fig. 11 *B*). Five hours after operation (fig. 11 *A*) the temperature had risen to 106 F., and 35 mg. of soluble pentobarbital given half intravenously and half subcutaneously, resulted in a fall to 103 F. On a subsequent rise to 104 F.,

35 mg. of soluble pentobarbital was twice administered subcutaneously, with no immediate effects, but with a gradual fall to 102 F. The animal's further course will be considered later.

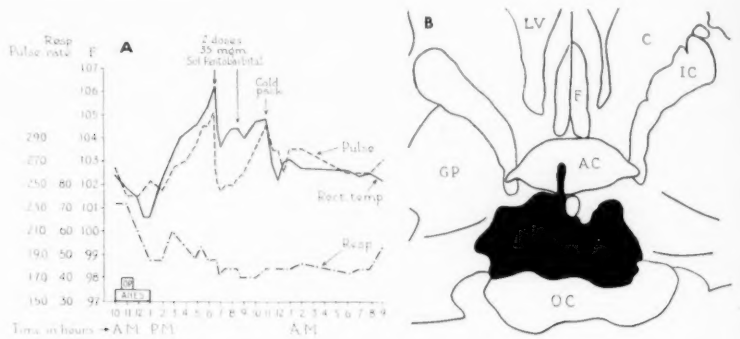

Fig. 10 (monkey 10).—*A*, temperature chart; *B*, lesions in the brain.

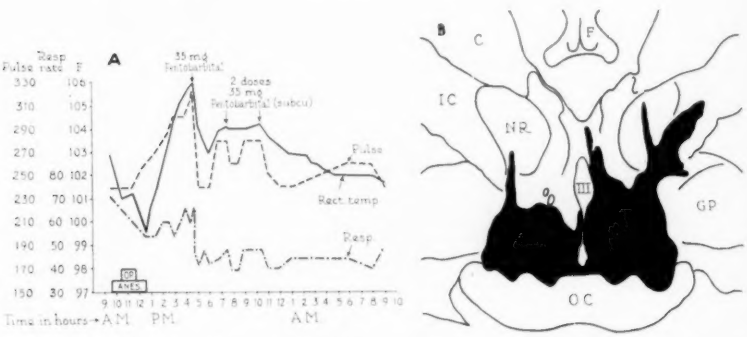

Fig. 11 (monkey 11).—*A*, temperature chart; *B*, lesions in the brain.

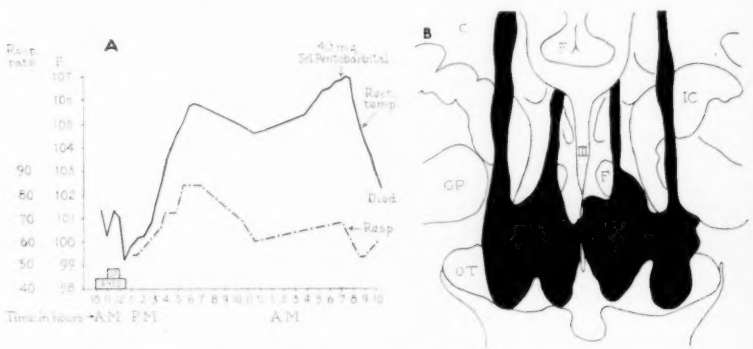

Fig. 12 (monkey 12).—*A*, temperature chart; *B*, lesions in the brain.

Monkey 12 suffered a large lesion of the anterior and tuberal parts of the hypothalamus (fig. 12 *B*). Six hours after operation (fig. 12 *A*) the temperature had risen to 105.9 F., from which point it gradually fell to 104.6 F. and then slowly

rose to reach 107 F. nineteen hours after operation. Then 40 mg. of soluble pentobarbital was administered intraperitoneally, and though the temperature fell to 102.2 F., the animal died three and one-half hours later. Autopsy showed no gross pathologic change, and death was attributed to the hyperthermia, which apparently was allowed to proceed for too long a time and to too high a level before treatment.

These animals taken as a group provide a clearcut demonstration of the efficacy of soluble pentobarbital as a therapeutic agent in reducing and controlling acute neurogenic hyperthermia. It is thought that the single fatality, that of monkey 12, to which pentobarbital was not administered until nineteen hours after operation, when the animal's temperature was 107 F., could have been avoided if the drug had been given earlier.

In monkeys 6 to 12 of this group, as well as in animals 4 and 5, piloerection and shivering were frequently noted during the course of the hyperthermia; the extremities remained cold, and no sweating occurred. The picture was one of paralysis of heat loss activity, with maintenance of action of heat conservation mechanisms. On administration of pentobarbital during the course of the hyperthermia, it was repeatedly observed that piloerection was relaxed, shivering ceased and the extremities became warm after injection. It seems clear, therefore, that at least a part of the effect of pentobarbital in reducing hyperthermia is to be attributed to its suppression of heat conservation activity. It may be pointed out, also, that in each experiment the hyperthermia was associated with an increase in the pulse and usually in the respiratory rate, alterations indicative of an increase in the metabolic processes of the body. It is not certain whether this increase was the cause or the result of the rise in body temperature, but it can be seen from the charts that in each case, after the injection of pentobarbital, the pulse and respiratory rates fell notably, and before body temperature had shown a great decline. It seems likely that, in addition to its suppression of heat conservation, pentobarbital also suppresses heat production.

The doses of soluble pentobarbital effective in reducing experimental hyperthermia were not large, 30 and 40 mg. in monkeys weighing 3 to 3.75 Kg. giving good results. These doses amount to approximately 10 to 12 mg. per kilogram, and are roughly one third of the usual dose of soluble pentobarbital required for surgical anesthesia in the monkey. The result in a single instance of injection of 52 mg. of soluble pentobarbital, or 17 mg. per kilogram, suggests that this quantity was somewhat excessive, for body temperature was reduced below normal. Three instances of subcutaneous injection, without effect or with only a very gradual fall in temperature, suggest that the constriction of peripheral vessels, which is one of the features of the hyperthermia, prevented or delayed the absorption of pentobarbital given subcutaneously and that intravenous or intraperitoneal injection is indicated.

Mild or Brief Hyperthermia.—In 7 experiments acute postoperative rises in temperature were encountered which either did not proceed as high or did not continue as long as in the experiments already presented. A group of 5 of these experiments may be distinguished in which lesions were placed in the preoptic region and the anterior portion of the hypothalamus, but in which the damage to the two halves of the brain was notably asymmetric. The animal which presented the highest rise in temperature of any of this group may be taken as an example.

In monkey 13 the lesion (fig. 13 *B*) was situated in the preoptic region and the anterior portion of the hypothalamus but was asymmetric, so that the entire medial part of the left side and much of the lateral portion of the right side of this region were spared. The temperature rose abruptly (fig. 13 *A*), to reach 105.8 F. three and one-half hours after operation, and then declined, to reach normal limits seven hours after operation. In the other animals with asymmetric

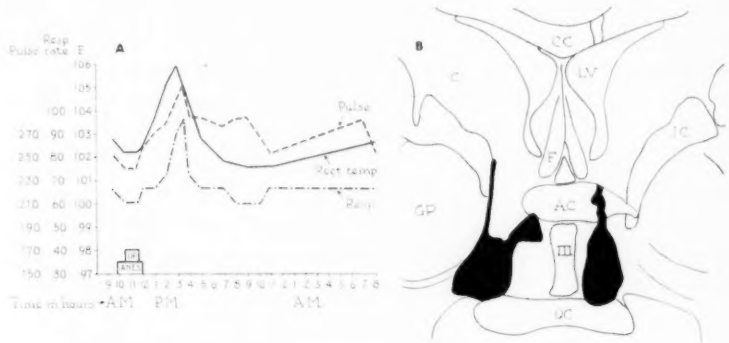

Fig. 13 (monkey 13).—*A*, temperature chart; *B*, lesions in the brain.

lesions the rises in temperature were not as high, the peaks being 105.4, 105, 104.9 and 103 F. respectively.

It seems reasonable to ascribe the mild nature of the hyperthermia in this group of animals to incomplete destruction of the bilaterally distributed mechanism for heat loss as a result of the asymmetric position of the lesions. In the 2 remaining animals the absence of marked and prolonged hyperthermia could be attributed to associated impairment of heat conservation facilities as a result of coincident injury to more caudal regions of the hypothalamus.

In monkey 14 the lesion was located more caudally than in the animals already considered, in the tuberal region of the hypothalamus (fig. 14 *B*). The animal's temperature (fig. 14 *A*) was not maintained well during the course of the operation and at its conclusion was only 97 F. The temperature climbed rapidly to within normal limits and then increased gradually, to reach a peak of 103 F. eight hours after operation. It then declined to within normal limits. In a second similar case there was a rise to 104 F. Tests of temperature regulation in the chronic state will be given later.

Postoperative Hypothermia.—In 2 animals of the present series a progressive fall in body temperature was encountered after operation. The lesions in these animals with hypothermia were subsequently observed to be located more caudally than was intended, in the tuberal and the anterior mamillary region of the hypothalamus. Monkey 15 is an example.

In monkey 15 the lesion was situated in the tuberal part of the hypothalamus (fig. 15 *B*) and extended backward to terminate above the mamillary bodies.

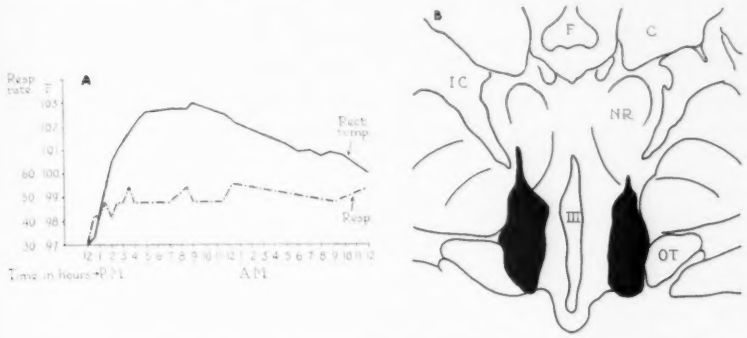

Fig. 14 (monkey 14).—*A*, temperature chart; *B*, lesions in the brain.

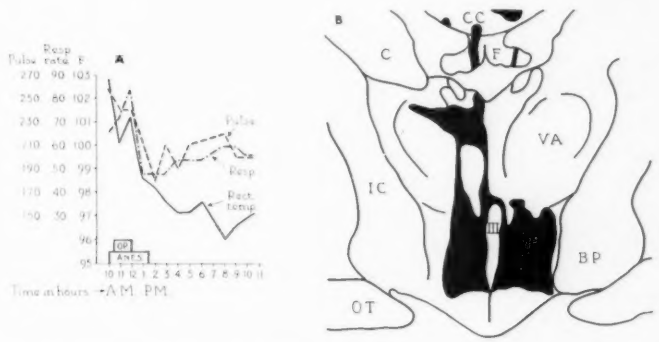

Fig. 15 (monkey 15).—*A*, temperature chart; *B*, lesions in the brain.

The animal's temperature (fig. 15 *A*) was 101.2 F. at the conclusion of the operation. When the animal was placed in a room at 80 F., its body temperature fell to 98.5 F. during the period of recovery from the ether anesthesia. Then, instead of rising to a normal level, as in the control animals, or becoming further elevated, as in the animals with hyperthermia, this animal's temperature continued to fall gradually, and from eight to ten hours after operation it ranged between 96 and 97 F., even though artificial heat was applied. The deficient temperature regulation in the chronic state will be discussed later.

General Consideration of the Acute Postoperative Results.—Before proceeding further, it is of interest to assemble the observations during

the acute postoperative period and to consider them from the point of view of the distribution of the lesions in the preoptic region and the hypothalamus. In each case the area of the lesion was projected on a reconstruction of the midsagittal plane; the projections from 2 control animals (monkeys 1 and 2), from all of the animals with severe hyperthermia (monkeys 4 to 12) and from an animal with postoperative hypothermia (monkey 15) are shown together in figure 16 *A*.

The lesions in hyperthermic monkeys 4 to 12 (shaded in figure 16 *A*) are seen to be clustered in the preoptic region and the anterior portion of the hypothalamus and to be distributed chiefly between the anterior commissure and the optic chiasm. Since destruction of this region was followed by a severe postoperative rise in temperature, in the course of which heat loss activity remained paralyzed, it is reasonable to conclude

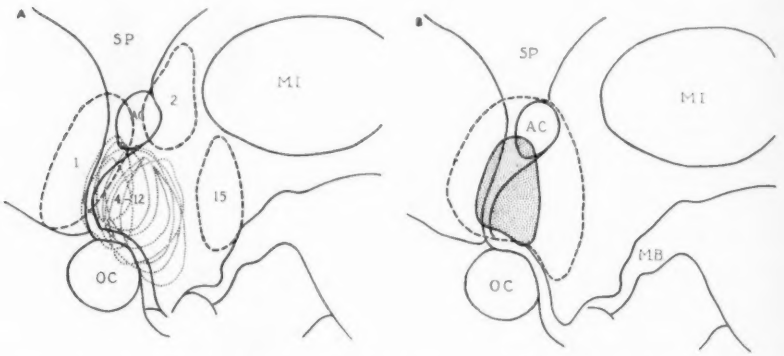

Fig. 16.—*A*, outlines of lesions in the brains of monkeys 1, 2, 4 to 12 and 15 projected on a drawing of a medial sagittal section of the brain.

B, projection on a medial sagittal section of a monkey's brain of the center which responds to local heating by activating the heat loss mechanisms. The stippled area represents the main part of the center, which is surrounded by a less active region enclosed by the broken line.

that within this region are situated neural mechanisms essential for the initiation and regulation of processes for body cooling.

Further evidence for this view, derived from a different experimental approach, is presented in figure 16 *B*, which depicts as projected on the midsagittal plane the region of the monkey's brain the local heating of which results in activation of heat loss mechanisms. It has been shown by Beaton, McKinley, Berry and Ranson[11] that in the anesthetized monkey warming this region with high frequency current passed between

11. Beaton, L. E.; McKinley, W. A.; Berry, C. M., and Ranson, S. W.: Localization of Cerebral Center Activating Heat-Loss Mechanisms in Monkeys, J. Neurophysiol. **4**:478-485, 1941.

the tips of otherwise insulated electrodes results in excess sweating, vasodilatation and accelerated respiration, which give every appearance of being identical with the integrated response of the normal animal to an elevated environmental temperature. The reconstructed aspect of this heat-sensitive area (fig. 16 *B*), not hitherto presented, is included here for comparison with the distribution of lesions which, in monkeys 4 to 12 of the present investigation (fig. 16 *A*), were followed by severe postoperative hyperthermia. The distribution of the two regions coincides closely, and the two lines of evidence complement one another in a fashion which points to a single conclusion, namely, that the preoptic region and the anterior region of the hypothalamus are the site of a center for heat loss.

It seems clear that the hyperthermia which followed injury to the preoptic region and the anterior end of the hypothalamus in these experiments is to be attributed to the destruction of a specific neural mechanism for heat loss located within this area, and not to the interruption of long pathways which might simply be passing through this part of the brain from other levels. Lesions in monkeys 1 and 2, located anterior and dorsal to the preoptic region and the anterior part of the hypothalamus (fig. 16), were not followed by hyperthermia, nor did hyperthermia follow the laterally placed lesions in monkey 3 (fig. 3). The caudal lesion in monkey 15 (fig. 16 *A*) was followed by postoperative hypothermia, due, undoubtedly, to injury of the heat conservation mechanism, which Ranson, Fisher and Ingram [12] and Ranson [13] have shown to be most effectively thrown out of function by lesions of the posterior portion of the hypothalamus.

Descending pathways from the anterior portion of the hypothalamus were also interrupted by the lesions in monkey 15, and the animal exhibited chronic impairment in the ability to defend itself against overheating. This result suggests that there is more to the etiology of hyperthermia than simply the destruction of the heat loss mechanism. Pertinent observations derived from tests for temperature regulation in the chronic state made on all surviving monkeys may be presented before the problem is considered further.

TEMPERATURE REGULATION IN THE CHRONIC STATE

Control Animals.—As has already been mentioned, monkeys 1, 2 and 3, with lesions anterior, dorsal and lateral, respectively, to the preoptic region and the anterior portion of the hypothalamus, showed

12. Ranson, S. W.; Fisher, C., and Ingram, W. R.: Hypothalamic Regulation of Body Temperature in the Monkey, Arch. Neurol. & Psychiat. **38**:445-466 (Sept.) 1937.

13. Ranson, S. W.: Regulation of Body Temperature, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:342-399, 1940.

no impairment in temperature regulation in the chronic state. When tested from four to five weeks after operation, they exhibited good piloerection and violent shivering on exposure to cold and profuse sweating on exposure to heat, at thresholds of body temperature which were similar to those encountered in preoperative tests.

Animals with Severe Hyperthermia.—Five of the monkeys with severe hyperthermia in the acute postoperative period were tested in the chronic state. Two of these animals showed chronic impairment in the ability to defend themselves against overheating, with maintained, though not perfectly normal, ability to guard against excessive cooling.

Monkey 11, with the large lesion in the anterior portion of the hypothalamus, shown in figure 11, was kept for five weeks after operation. During this time the animal showed a tendency to a slightly subnormal or considerably elevated temperature, according to whether the environmental temperature was low or high. The temperature regulation was tested on two occasions, three and five weeks after operation. At both trials the animal showed marked piloerection and vigorous shivering on exposure to cold, but on neither occasion did it sweat or exhibit vasodilatation on exposure to heat, even though the rectal temperature was elevated in the trials to 105.5 and 105.7 F. Similar results were encountered in monkey 10.

The 3 remaining animals with initial severe hyperthermia, monkeys 7, 8 and 9, showed normal regulation to both heat and cold in the chronic state. The lesions in these animals (figs. 7 to 9) were small, sparing some of the lateral and a considerable amount of the medial part of the preoptic region. When the lesion was viewed in reconstruction, it was evident, also, that the injury did not extend as far caudally into the anterior portion of the hypothalamus as did the larger lesions in monkeys 10 and 11. It is suggested that the heat loss mechanism was initially thrown completely out of function by the partial destruction of the preoptic region and the anterior portion of the hypothalamus in monkeys 7, 8 and 9, but that the margin of safety in this mechanism was sufficiently great for the remaining parts to maintain normal heat loss function in the chronic state. The enduring paralysis of heat loss activity with the more extensive destruction of the preoptic region and the anterior portion of the hypothalamus in monkeys 10 and 11 argues against a compensatory function being assumed by some other part of the brain.

Animals with Mild Hyperthermia.—Normal or only slightly subnormal heat regulation in the chronic state in the 5 monkeys with asymmetric lesions of the preoptic region and the anterior portion of the hypothalamus, of which monkey 13 (fig. 13) is an example, also suggests that while partial injury to the heat loss mechanism is sufficient to impair its function more or less completely in the acute period, in the chronic state the uninjured parts will maintain normal, or almost normal, activity.

Monkey 14, as well as a second similar animal, which exhibited mild hyperthermia after symmetrically placed lesions in the tuberal portion of the hypothalamus (fig. 14), maintained normal body temperatures under laboratory

conditions during its survival of five weeks. Tests of regulation against heat made two and five weeks after operation showed complete loss of sweating, though the body temperature was elevated to 106.1 F. in both trials. A test of regulation against cold five weeks after operation showed an impaired reaction, with only slight piloerection and shivering. The paralysis of heat loss function, which remained as extreme as in the animals with destruction of the preoptic region and the anterior portion of the hypothalamus, indicates that the mechanism for heat loss either extends into the tuberal part of the hypothalamus or sends its efferent pathway backward through the lateral part of this region. This animal's failure to exhibit more pronounced hyperthermia in the acute postoperative period may be attributed to the coincident injury of the heat conservation mechanism, indicated by its impaired regulation against cold in the chronic state.

Animals with Postoperative Hypothermia.—Monkey 15, and a second similar animal, which exhibited acute postoperative hypothermia after lesions of the tuberal and anterior mamillary parts of the hypothalamus (fig. 15), did not regain the ability to keep the body temperature up to the normal level under ordinary laboratory conditions. During a survival of three weeks monkey 15, which was kept much of the time in an incubator at 86 F., frequently exhibited temperatures as low as 95 F. No shivering or piloerection was ever observed, even in response to extreme cold. On exposure to heat three weeks after operation, reddening of the chest was noted, but no sweating occurred, though the body temperature was elevated to 105.5 F. In the second animal neither sweating nor vasodilatation occurred, though the animal's temperature was elevated to 106.8 F.

The paralysis of heat loss activity in these 2 animals may be attributed to interruption of the efferent pathway for heat loss descending from more anterior levels of the hypothalamus. It seems unlikely that the heat loss mechanism itself extends into the caudal part of the hypothalamus, for heat loss activity may be abolished by more anterior lesions, which leave the caudal portion of the hypothalamus intact (see report on monkey 11). With the heat loss mechanism paralyzed, the failure of monkey 15 and its mate to exhibit postoperative hyperthermia may be ascribed to coincident paralysis of the heat conservation mechanism, the activity of which appears essential for the acute postoperative elevation in temperature. When the latter mechanism was infringed on by tuberal lesions (monkey 14), only mild hyperthermia resulted. When it was destroyed (monkey 15), not only did the temperature fail to rise after operation, but hypothermia resulted. In another paper evidence was presented to show that hypothermia regularly results from bilateral lesions in the posterior part of the hypothalamus (Ranson [18]).

The fall of body temperature after a lesion in the posterior portion of the hypothalamus and that after the injection of pentobarbital appear to have a common basis, a block of the heat conservation mechanism.

This raises the question whether the antipyretic action of pentobarbital may not be effected at the hypothalamic level. Without any rash commitments, it can be pointed out that Fulton,[14] Masserman [15] and Hodes and Magoun [16] have reported a decrease of hypothalamic excitability during anesthesia induced with pentobarbital.

COMMENT

At least two factors appear to be operative in the production of postoperative hyperthermia. First, the heat loss mechanism must be thrown out of function. Second, and just as important, the heat conservation mechanism must retain its activity. In these experiments, observations on the monkeys revealed increased activity of the heat conservation mechanism during hyperthermia, but this increase was not always maximal or continuous. Coldness of the extremities was an enduring feature; piloerection and shivering occurred only intermittently and were never extreme in degree. The question, therefore, may be raised whether a third factor, that of increased heat production, is also operative during the period of hyperthermia. Calorimetric tests would be necessary for a definite answer to this question, but observation of increased pulse and respiratory rates, indicative of increased metabolic activity, is suggestive. If increased heat production is an essential part of severe hyperthermia, it, too, would appear to be dependent on the integrity of the caudal part of the hypothalamus.

Little attention has heretofore been directed to the reasons for the disappearance of the acute postoperative hyperthermia. The increased activity of the heat conservation, and possibly also of the heat production mechanism, which appears to be the active feature of this disorder, is for some reason only short lasting. In the surviving animals in the present study, the elevation of body temperature never persisted beyond the second postoperative day. Its abatement is not necessarily to be ascribed to recovery of heat loss activity, for in acutely hyperthermic monkeys 10 and 11 the paralysis of this activity endured for several weeks. It is possible that surrounding the lesions which destroy the heat loss mechanism in the preoptic region and the anterior portion of the hypothalamus is a zone extending into the posterior part of the hypothalamus in which edema, or a concentration of breakdown products, or some other unknown agent, exerts a short-lasting (one or

14. Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1938.

15. Masserman, J. H.: Effects of Analeptic Drugs on the Hypothalamus of the Cat, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:624-634, 1940.

16. Hodes, R., and Magoun, H. W.: Autonomic Responses to Electrical Stimulation of the Forebrain and Midbrain with Special Reference to the Pupil, J. Comp. Neurol. **76**:169-190, 1942.

two day) irritation. It is also possible that reciprocal inhibitory connections exist between the hypothalamic mechanism for heat loss and that for heat conservation, so that destruction of the first is associated with exaggerated activity of the second, as a short-lasting release phenomenon.

The present study has provided ample demonstration in monkeys of a sharp postoperative rise in body temperature following injury to the anterior region of the hypothalamus. During the rise in temperature there are absence of sweating, a warm trunk but cold extremities, pronounced tachycardia and some hyperpnea and intermittent piloerection and shivering. If the animal is left untreated, the temperature may rise to a fatal level. The disorder constitutes acute neurogenic hyperthermia, and we see no reason to distinguish it from the hyperthermia which frequently follows acute injury to the hypothalamic region in man.

The evidence points to a twofold cause of experimental hyperthermia. The disorder involves, first, paralysis of the central mechanism for heat loss and, second, the maintained or increased activity of the central mechanism for heat conservation, and perhaps also for heat production. The combination of these conditions results in an elevation of body temperature which the animal is powerless to dissipate. The normal balance of the temperature-regulating mechanisms is lost, and the scale is weighted toward the side of heat conservation and heat production. Attempts to control the disorder by the administration of central-acting antipyretics which normally excite the heat loss mechanism might be expected to fail, because paralysis of the central mechanism for heat loss is one of the precipitating features of the condition.

Compelling evidence has been presented in this study for the value of soluble pentobarbital in reducing and controlling experimental hyperthermia. The administration of pentobarbital appears to correct the imbalance in the temperature-regulating mechanisms by suppressing the activity of the mechanism for heat conservation and heat production. After injection of soluble pentobarbital during hyperthermia in these experiments, piloerection was relaxed and shivering ceased; the cold extremities became warm, and the pulse and respiratory rates were decreased. The body temperature fell to a normal level, or, with greater concentrations of pentobarbital, to a subnormal level. A single injection of soluble pentobarbital was effective in reducing body temperature for a period of only three to six hours, but because the effective doses were of hypnotic, rather than of anesthetic, concentration, repeated doses could be administered.

We should like to suggest that the striking efficacy of soluble pentobarbital in reducing experimental hyperthermia in the monkey warrants

its trial in the treatment of neurogenic hyperthermia following acute injury to the brain in man, the incidence of which in these times may be expected to be increased.

SUMMARY

Bilateral injury to the rostral region of the hypothalamus in a series of monkeys results in an acute postoperative rise in body temperature, which if untreated proceeds to a fatal level.

This experimental hyperthermia is the result of central paralysis of the heat loss mechanism, associated with maintained or exaggerated activity of the central mechanism for heat production and heat conservation.

Intravenous administration of soluble pentobarbital (pentobarbital sodium) during the course of the hyperthermia suppresses the activity of the mechanism for heat conservation and heat production and reduces body temperature to the normal level. When administered subcutaneously, pentobarbital is relatively ineffective.

The striking efficacy of pentobarbital in reducing experimental hyperthermia in the monkey warrants its trial in the treatment of neurogenic hyperthermia following acute injury to the brain in man.

303 East Chicago Avenue.

MYASTHENIA GRAVIS

CURARE SENSITIVITY; A NEW DIAGNOSTIC TEST AND APPROACH TO CAUSATION

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OMAHA
AND
CAPTAIN PAUL T. CASH
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In previous investigations [1] with standardized curare [2] one of us (A. E. B.) has called attention to the similarity of the action of curare and the symptoms of myasthenia gravis. After these clinical observations we discovered the same hypothesis had been suggested by others: Oppenheim [3] in 1901 observed that "veratrine evoked in muscles a condition analogous to myasthenia"; Briscoe [4] in 1936 showed that mild curarization produced a myogram similar to that of myasthenia gravis, and later Harvey and his co-workers [5] confirmed this similarity and stated, "The characteristic abnormalities of the electrical responses of the myasthenic and curarized muscle are identical in all respects." From the analogy between myasthenia gravis and partial curarization he sug-

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Read at the Sixty-Eighth Annual Meeting of the American Neurological Association, Chicago, June 5, 1942, and presented as a motion picture (scientific exhibit) before the Section on Nervous and Mental Diseases at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Bennett, A. E.: Curare: A Preventive of Traumatic Complications in Convulsive Shock Therapy, Am. J. Psychiat. **97**:1040 (March) 1941; Clinical Investigations with Curare in Organic Neurologic Disorders, Am. J. M. Sc. **202**: 102 (July) 1941.

2. E. R. Squibb & Sons furnished the standardized curare used in these experiments. We have also been using crystalline curare, described by O. Wintersteiner and J. D. Dutcher (Science **95**:10 [May 1] 1942).

3. Oppenheim, H.: Die myasthenische Paralyse, Berlin, S. Karger, 1901, p. 107.

4. Briscoe, G.: The Antagonism Between Curarine and Prostigmin and Its Relation to the Myasthenia Problem, Lancet **1**:469 (Feb. 29) 1936.

5. Harvey, A. M., and Masland, R. L.: The Electromyogram in Myasthenia Gravis, Bull. Johns Hopkins Hosp. **69**:1 (July) 1941. Harvey, A. M., and Lilienthal, J. L.: Observations on the Nature of Myasthenia Gravis, ibid. **69**:566 (Dec.) 1941.

gested the hypothesis that a circulating inhibitor substance may arise from the thymus gland. Harvey and his associates [6] concluded:

> All of the experimental work, therefore, points to the similarity of myasthenia to a mild curarization; it thus seems likely that the defect in the disease, as in curarization, is due to an elevation of the threshold of the motor end-plates to the effects of the nerve impulses reaching them.

In myasthenia gravis there is some interference in transmission of nerve impulses across the myoneural junction; there may also be some disorder of muscle metabolism. Since acetylcholine (Dale, Feldberg and Vogt [7]) is the chemical mediator of neuromuscular transmission, some abnormality in the action of acetylcholine seems likely in myasthenia gravis. Physostigmine (Walker [8]), which restores normal neuromuscular performance in most myasthenic patients, is known to hinder destruction of acetylcholine by choline esterase. There seems to be no direct evidence that acetylcholine is lacking or destroyed in cases of myasthenia. We have found that intravenous administration of acetylcholine does not improve myasthenic symptoms; this suggests there is no deficiency of acetylcholine in myasthenia gravis. However, Lanari,[9] giving acetylcholine intra-arterially, obtained contraction of myasthenic muscle. There is no increase in choline esterase either in the serum or in muscle to account for an increased destruction of acetylcholine. Therefore the evidence of any deficiency of acetylcholine in the disease is inconclusive.[10]

Keisser and Neuschlab [11] demonstrated that curare inhibits the action of acetylcholine. The principle of the antagonistic action of curare and acetylcholine on a frog gastrocnemius muscle preparation can be used as a method of assay of the potency of curare. According to Holaday, addition of acetylcholine to a frog gastrocnemius muscle preparation produces a contraction which if recorded isometrically furnishes a reference height for comparison with a decreased height of contraction obtained through the inhibitory effect of a solution of curare. Curare thus seems to raise the threshold of muscle contraction to acetylcholine; according to

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6. Gammon, G. D.; Harvey, A. M., and Masland, R. L.: On the Nature of Certain Diseases of the Voluntary Muscles, Biological Symposia, Lancaster, Pa., Jacques Cattell Press, 1941, vol. 3, pp. 292-297.

7. Dale, H. H.; Feldberg, W., and Vogt, M.: Release of Acetylcholine at Voluntary Motor Nerve Endings, J. Physiol. **86**:353 (May 4) 1936.

8. Walker, M. B.: Case Showing Effect of Prostigmin on Myasthenia Gravis, Proc. Roy. Soc. Med. **28**:759 (April) 1935.

9. Lanari, A.: A Pharmacologic Study of the Myotonic Muscle, Arch. internat. de pharmacodyn. et de thérap. **61**:360 (March 31) 1939.

10. McGeorge, M.: Choline Esterase Activity in Disease, with Special Reference to Myasthenia Gravis, Lancet **1**:69 (Jan. 9) 1937.

11. Keisser, O., and Neuschlab, S. M.: Antagonism of Acetylcholine and Curare, Arch. f. exper. Path. u. Pharmakol. **91**:356, 1921.

Harvey, it inhibits muscular action by altering the threshold of muscle response to acetylcholine. These observations have also been reported in experiments by Hodes and Steiman.[12] Harris and Harris[13] found that very small amounts of curare have a pronounced inhibitory effect on choline esterase activity of human serum; this observation has been confirmed by other investigators.[13a] Chronaxia is increased both in myasthenic and in curarized muscle according to Djuricic and Vujic.[14] After injection of prostigmine methylsulfate it is decreased.

There is some evidence in favor of an additional primary disturbance of muscle metabolism. There is a decided increase in potassium in myasthenic muscles according to Cumings[15]; prostigmine produces a fall in the amount of muscle potassium, with a rise in the potassium of the serum and the red blood cells but with no increase in urinary excretion. The administration of potassium in large amounts benefits myasthenic patients. An increased potassium ion concentration tends to improve conduction at nerve terminals in voluntary muscle. Ephedrine and guanidine hydrochloride[16] seem to increase the sensitivity of striate muscle to acetylcholine and to relieve the asthenia and paretic symptoms of the disease but do not affect choline esterase activity. Stare and Ricketts[17] found that myasthenic muscles consume less oxygen than do normal muscles. Injection of prostigmine methylsulfate increases the consumption of oxygen, which suggests some abnormality in intermediary metabolism.

Other evidence of primary muscle disorder in the disease is suggested by Milhorat's[18] observations that with advanced stages of myasthenia

12. Hodes, R., and Steiman, S. E.: The Effects of Acetylcholine and Eserine on Frog Muscle, Am. J. Physiol. **127**:470-479 (Oct.) 1939.

13. Harris, M. M., and Harris, R. S.: Effect in Vitro of Curare and Beta-Erythroidin Hydrochloride on Choline Esterase of Human Blood Serum, Proc. Soc. Exper. Biol. & Med. **46**:619 (April) 1941.

13a. A. R. McIntyre and R. E. King (D Tubocurarine Chloride and Choline Esterase, Science **97**:69 [Jan. 15] 1943) found that all crude curare preparations examined inhibit serum choline esterase, while the chemically pure (D tubocurarine chloride) preparation is devoid of this action. The inhibitory activity of crude curare preparations on choline esterase is not necessarily related to their paralytic action.

14. Djuricic, I., and Vujic, V.: Contributions to the Problem of Therapy in Myasthenia Gravis Pseudoparalytica, Arch. f. Psychiat. **111**:48 (Jan. 10) 1940.

15. Cumings, J. N.: Potassium and Muscular Disorders, J. Neurol. & Psychiat. **4**:226 (July-Oct.) 1941.

16. Minot, A. S.; Dodd, K., and Riven, S. S.: Use of Guanidine Hydrochloride in Treatment of Myasthenia Gravis, J. A. M. A. **113**:553 (Aug. 12) 1939.

17. Stare, F. J., and Ricketts, H. T.: The in Vitro Respiration of Muscle in Myasthenia Gravis, personal communication to the author.

18. Milhorat, A. T.: Studies in Diseases of Muscle, Arch. Neurol. & Psychiat. **46**:800 (Nov.) 1941.

prostigmine has practically no effect or else increasing amounts are necessary to depress the choline esterase to lower levels. This phenomenon was limited to the response of voluntary muscles, which became increasingly refractory to stimulation. No diminishing effect of prostigmine on the activity of choline esterase was demonstrated. In the terminal stages of myasthenia patients showed serious involvement of creatine metabolism, which had been normal before. For these patients administration of prostigmine was ineffective; in other seriously ill patients who responded to prostigmine the creatine was normal.

None of these mechanisms is completely understood. According to Goodman and Gilman:[19]

> The pathological physiology of myasthenia may be due to: (1) a deficiency in the amount of acetylcholine produced at motor nerve endings, (2) an increase in muscle choline esterase, and (3) the existence of some abnormal substance or metabolite with a curare-like action which elevates the threshold of skeletal muscle to the effects of nerve stimuli; which of these factors is involved is not known.

Because curarization produces all the manifestations of myasthenia and myasthenic patients are exceedingly sensitive to the drug, it appears likely that some foreign substance similar in chemical action to curare initiates myasthenia by inhibiting or neutralizing the action of acetylcholine.

Quinine, which has a weak curare-like action, also aggravates myasthenia and relieves the opposite condition, myotonia congenita. Milhorat expressed the opinion that the action of quinine suggested the nature of the disease and could be used in diagnosis; this confirms our contention, but the specific action of standardized curare is more accurate. Harvey[20] and we[21] have likewise demonstrated that quinine methochloride produces a myasthenic reaction, the effects of which are relieved by prostigmine.

The pharmacologic action of curare is entirely on the neuromuscular junction; it inhibits, anatognizes or blocks acetylcholine and practically abolishes the transmission of nerve impulses. Physostigmine is a specific antidote for curare intoxication. The symptoms produced in the patient by varying doses of curare are exactly those of myasthenia gravis; they progress according to dosage, just as myasthenia progresses from mild to severe stages and end in paralysis of the respiratory muscles. In other words, curare poisoning produces artificial myasthenia gravis.

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19. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, p. 342.

20. Harvey, A. M.: The Action of Quinine Methochloride on Neuromuscular Transmission, Bull. Johns Hopkins Hosp. **66**:52 (Jan.) 1940.

21. Bennett, A. E., and Cash, P. T.: Curarization with Quinine Methochloride to Prevent Traumatic Complications of Metrazol Shock Therapy, Psychiatric Quart. **15**:351 (April) 1941.

These observations indicate that the myasthenic patient would exhibit an increased degree of sensitivity to curare. We have found this to be true. In 5 patients with myasthenia gravis, all showing decidedly different stages of the disease, we found that one twentieth to one fifth (5 to 15 mg.) of the average adult dose of standardized curare necessary to produce generalized paresis in a normal subject causes profound exaggeration of symptoms in myasthenic patients. The results of these studies have been recorded in motion pictures. From these observations we have concluded that curare can be safely used as a specific diagnostic test for myasthenia gravis, just as prostigmine methylsulfate [22] is now used in the opposite direction, but is not always conclusive. In doubtful cases in which the response to the prostigmine test is indefinite we believe curare will produce a more specific reaction.

These observations suggest that the etiologic agent in myasthenia gravis is some form of curare intoxication. Possibly with overactivity of the thymus gland there is elaborated a substance which has a curare-like action, similar to that of thyroxin in exophthalmic goiter. The evidence for this assumption is the fairly constant pathologic observation at necropsy of enlargement or tumor of the thymus,[23] the relief of myasthenia by irradiation of the thymus and thymectomy [24] and Adler's[25] observations on experimental muscular weakness resembling myasthenia in young animals with thymus gland transplants. These symptoms were relieved by prostigmine. Adler also produced asthenia with extracts of the thymus gland. Indirect evidence is the common association of exophthalmic goiter and myasthenia.[26] Mild myasthenia occurs in cases of exophthalmic goiter, in which it is known that the thymus gland hypertrophies. Both myasthenia and hyperthyroidism have been relieved by thyroidectomy.[27] Some investigators, disagreeing with the thymus

22. Viets, H. R., and Schwab, R. S.: Prostigmin in the Diagnosis of Myasthenia Gravis, New England J. Med. **213**:1280 (Dec. 26) 1935.

23. Miller, H. G.: Myasthenia Gravis and the Thymus Gland, Arch. Path. **29**: 212 (Feb.) 1940. Blalock, A.: Tumors of the Thymic Region and Myasthenia Gravis, Am. J. Surg. **54**:149 (Oct.) 1941.

24. Blalock, A.; Mason, M. F.; Morgan, H. J., and Riven, S. S.: Myasthenia Gravis and Tumor of the Thymic Region, Ann. Surg. **110**:544 (Oct.) 1939. Blalock, A.; Harvey, A.; Ford, F. F., and Lilienthal, J. L.: The Treatment of Myasthenia Gravis by Removal of the Thymus Gland, J. A. M. A. **117**:1529 (Nov. 1) 1941. Campbell, E.; Fradkin, N. F., and Lipetz, B.: Myasthenia Gravis Treated by Excision of Thymic Tumor, Arch. Neurol. & Psychiat. **47**:645 (April) 1942.

25. Adler, H.: Thymus und Myasthenie, Arch. f. klin. Chir. **189**:529, 1937.

26. Cohen, S. J., and King, F. H.: Relation Between Myasthenia Gravis and Exophthalmic Goiter, Arch. Neurol. & Psychiat. **28**:1338 (Dec.) 1932.

27. Kowallis, G. F.; Haines, S. F., and Pemberton, J. deJ.: Goiter with Associated Myasthenia Gravis, Arch. Int. Med. **69**:41 (Jan.) 1942.

theory, have expressed the belief that the adrenals [28] are more likely responsible. It seems reasonable to believe that future studies of the causal agent responsible for myasthenia should be directed along neurophysiologic and biochemical lines in order to determine why myasthenic patients have chronic curare-like poisoning.

The following histories illustrate our experiments with curare in cases of myasthenia and suggest the technic and dosage of standardized curare that may be used as a specific diagnostic test.

CASE 1.—Mrs. V. P., aged 31, in 1939 had progressive difficulty in speaking; six months later dysphagia developed, together with remittent ptosis and diplopia. All the symptoms became progressive; the voice was inarticulate at times; great difficulty in movements of the tongue developed, and attempts to swallow caused choking spells. The trunk and extremities were uninvolved; a loss in weight of 25 pounds (11.3 Kg.) occurred.

Examination revealed undernutrition, bilateral ptosis, loss of upward conjugate movements of the eyes, expressionless facies, inability to elevate or completely protrude the tongue and almost complete anarthria. Otherwise, a complete examination revealed nothing abnormal.

Prostigmine Diagnostic Test.—Injection of 1.5 mg. of prostigmine methylsulfate with 1/100 grain (0.6 mg.) of atropine sulfate resulted in a 4 plus score, presumptive evidence of myasthenia gravis.

Curare Diagnostic Test.—The patient's weight was 100 pounds (45.4 Kg.). The average curarizing dose for a person of this weight would be 50 mg. (1 mg. per two pounds [1.8 Kg.]) of standardized curare to produce mild partial generalized motor paresis. One-tenth this dose, or 5 mg. of curare principle, was slowly injected intravenously over a period of one minute. Immediately at the end of injection the patient showed complete bilateral ptosis, external ophthalmoplegia, complete loss of all movements of the tongue, flaccid paresis of the muscles of the neck, almost complete flaccid paresis of all extremities and respiratory difficulty. The height of the reaction came about two minutes after injection, when 1.5 mg. of prostigmine methylsulfate with 1/100 grain (0.6 mg.) of atropine sulfate was injected intravenously. Within two minutes after the injection all evidence of acute curare intoxication was gone, and most of the myasthenic symptoms were relieved.

CASE 2.—J. L., a man aged 54, for about ten years had had recurrent attacks of ptosis and inability to move the eyeballs; the attacks gradually progressed in frequency and severity. For about one year the patient had been conscious of almost constant inability to focus the eyes or rotate the eyeballs. Recently he noticed bulging of the left eye, huskiness of the voice after excessive talking and difficulty at times in swallowing.

Examination revealed that the left eye was exophthalmic, with the lid practically immobile; it measured 17 mm. with the Luedde exophthalmometer and the right 12 mm.; the right eyelid could be raised slightly with compensatory action of the frontalis muscle. Both eyes were fixed centrally; no motility whatever could be elicited. The facies was smooth, with a typical myasthenic expression; otherwise, complete examination revealed nothing abnormal.

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28. Bomskov, C., and Milzney, G.: Involvement of the Thymus in Myasthenia Gravis Pseudoparalytica, Arch. Neurol. & Psychiat. **47**:488 (March) 1942; abstracted from Deutsche Ztschr. f. Chir. **254**:99 (Oct. 19) 1940.

Prostigmine Diagnostic Test.—The response was doubtful, and daily intramuscular injections of the drug and oral medication gave only slight temporary relief of the ocular symptoms. Additional therapy with guanidine and adrenal cortex extract with lecithin also gave no relief.

Curare Diagnostic Test.—Several intravenous injections of one-tenth to one-fifth the average dose of standardized curare were given. Since the patient weighed 160 pounds (72.6 Kg.), the average dose necessary to produce generalized curarization would have been 80 mg. One-tenth, or 8 mg., of standardized curare given

Fig. 1 (case 1).—*A*, myasthenic facies prior to injection of curare. *B*, appearance of patient (*A*) after injection of 7 mg. of standardized curare, showing complete external ophthalmoplegia and generalized paresis. *C*, relief of all effects of curare and symptoms of myasthenia by injection of prostigmine.

intravenously over a period of one minute produced a peak reaction two minutes later. There were marked exaggeration of symptoms, complete bilateral ptosis, pronounced dysarthria and weakness of the muscles of the neck and the extremities. Another test with 15 mg. of standardized curare produced profound generalized symptoms of myasthenia with respiratory embarrassment. Each test was terminated by injection of 1.5 mg. of prostigmine methylsulfate and $\frac{1}{100}$ grain of atropine

sulfate. The exaggerated effects of curare disappeared immediately, but the myasthenic symptoms remained the same.

Thymectomy was performed; the gland weighed 24 Gm. Unfortunately, pneumothorax developed, and the patient died thirty-six hours after operation.

The pathologic report by Dr. J. P. Tollman follows: "The tissue consisted of a rather thin fibrous stroma supporting lymphoid tissue. The lymphoid tissue showed numerous active secondary germinal centers in which mitosis was common. One or two thymic corpuscles were noted. There was no evidence of inflammation. Adipose tissue was rather abundant."

CASE 3.—C. M. L., a man aged 74, in 1939 began having attacks of diplopia at midday, which were relieved by a night's rest; bilateral ptosis appeared at about the same time, followed later by generalized fatigability and huskiness of the voice.

Examination about four months after the onset revealed bilateral ptosis; rapid fatigue of ocular movements could be produced, with almost complete external ophthalmoplegia and myasthenic facies, symptoms disabling to the patient.

Prostigmine Diagnostic Test.—Injection of 1.5 mg. of prostigmine methylsulfate resulted in a 4 plus score, with complete relief of all symptoms within ten minutes. For over two years this patient has been able to carry on full occupation. Oral use of prostigmine methylbromide gives complete symptomatic relief.

Curare Diagnostic Test.—The patient's weight, 140 pounds (63.5 Kg.), indicated that approximately 70 mg. of standardized curare was needed to produce partial curarization. Injection of one-tenth this dose, or 7 mg., of standardized curare intravenously produced complete bilateral ptosis, complete external ophthalmoplegia, weakness of the facial muscles and of the tongue, anarthria and generalized muscular paresis within one minute. At the peak of the reaction, within two minutes, the patient felt immobile and helpless. Prostigmine methylsulfate, 1.5 mg., was given intravenously. Within two minutes the effects of the curare and all myasthenic symptoms disappeared.

CASE 4.—E. E., a man aged 56, for one month prior to examination had noted drooping of the left eyelid at the end of the day and complete relief after a night's rest. The ptosis was gradually extending over longer periods each day.

Complete examination gave normal results except for slight ptosis of the right lid and more complete ptosis of the left lid. The patient's weight was 197 pounds (89.4 Kg.).

Curare Diagnostic Test.—Ten milligrams of standardized curare was given intravenously over a one minute period. Within two minutes a moderate degree of ptosis appeared on the right side and complete ptosis on the left, with bilateral weakness of the facial muscles typical of myasthenia; no other objective symptoms were noted. Prostigmine methylsulfate, 1.5 mg., given intravenously, rapidly cleared up the curare symptoms and all evidence of bilateral ptosis.

This patient presents a very early stage of myasthenia gravis and is being observed for further development of myasthenic symptoms before treatment is started. The specific response to the curare test, in our opinion, is conclusive evidence of myasthenia.

CASE 5.—Mrs. P. N., aged 37, in 1925 first noticed after swimming that her legs gave out while climbing a hill. Since that time there had been progressive weakness of both legs and arms. The fatigability was more noticeable after midday, but at times the patient would fall on mounting stairs or drop objects while carrying them. She had recently noted fatigue with reading and could read

better with one eye closed, but never had had diplopia or ptosis. Also, there was fatigue on chewing, but never dysarthria or dysphagia. All symptoms were relieved one week prior to and one week after menstruation. Dyspnea on exertion and postmalleolar edema were other complaints.

Examination.—Complete physical and neurologic examinations revealed nothing abnormal except for a slight suggestion of bilateral weakness of the facial muscles. No fatigability of ocular muscles could be elicited. Repeated muscular tests of the

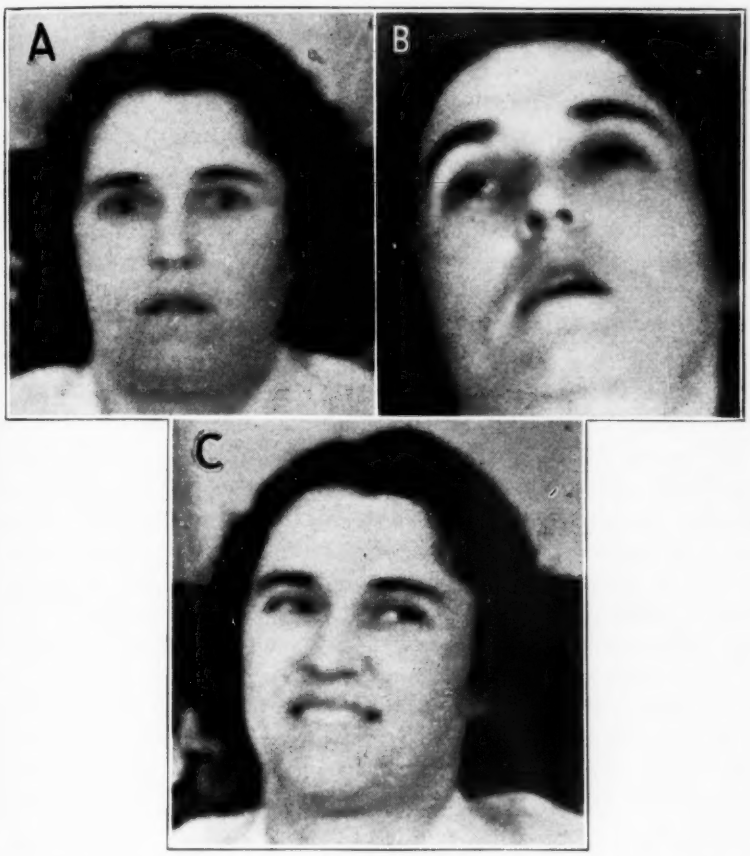

Fig. 2 (case 5).—*A*, myasthenia, of twelve years' duration, the asthenia being limited to the extremities. *B*, appearance after injection of 5 mg. of standardized curare, showing complete ophthalmoplegia and generalized paresis. *C*, relief of all effects of curare and myasthenic symptoms by injection of prostigmine.

upper and lower extremities elicited subjective fatigability; electrical stimulation did not induce the Jolly reaction.

Curare Diagnostic Test.—The patient weighed 124 pounds (56.2 Kg.); 5 mg., or one-twelfth the physiologic dose, of standardized curare was given intra-

venously. Within one minute the patient showed bilateral ptosis, external ophthalmoplegia, facial weakness, dysarthria and complete flaccid paresis of the head and the upper and lower extremities. After two minutes 1.5 mg. of prostigmine methylsulfate with 1/100 grain of atropine sulfate was given intravenously. Within two minutes all effects of curare and myasthenic symptoms disappeared.

Comment.—Patient 1 was severely disabled with myasthenia. Patient 2 had involvement almost limited to the ocular muscles in an unusual case of unilateral exophthalmos. Patient 3 had a mild form of the disease, which was completely controlled by prostigmine methylsulfate. Patients 1 and 3 gave strongly positive diagnostic reactions to prostigmine, but patient 2 gave an indifferent response and received no relief from any drug therapy. Patient 4 had a very early stage of myasthenia, for which the curare test enabled immediate diagnosis. Patient 5 presented an unusual case, since myasthenic symptoms extending over a twelve year period were confined to the larger muscles of the limbs and the shoulders, arms and legs, with practically no involvement of muscles of the oculomotor or the bulbar group. The curare test immediately brought out all the missing symptoms and clinched the diagnosis. After one-tenth the physiologic dose of curare, all 5 patients reacted specifically, with profound exaggeration of myasthenic symptoms, proof of the specificity of the active curare principle in the causation of the disease.

Technic of Curare Diagnostic Test.—About 1 mg. per kilogram of body weight of a standardized curare principle [2] administered intravenously produces mild generalized curarization in a normal adult. One-tenth this estimated physiologic dose is injected intravenously over a one minute period into the patient suspected of having myasthenia. Within two minutes after the injection the peak reaction occurs. If the patient has myasthenia, the existing myasthenic symptoms are aggravated, especially paralysis of the oculomotor muscles, weakness of the facial muscles and of the tongue, dysarthria and dysphagia. New symptoms may appear, such as flaccid paresis of the neck and extremities. The patient may be unable to speak or protrude the tongue and respiration of the diaphragmatic type may become labored. The test is to be terminated within two to three minutes by intravenous injection of 1.5 mg. of prostigmine methylsulfate with 1/100 grain of atropine sulfate; within a minute all acute effects of curare disappear, and if the patient is reactive to prostigmine the myasthenia symptoms likewise disappear. Larger doses of standardized curare, up to one-fifth the physiologic dose, may be given but are unnecessary for diagnosis. Without the use of prostigmine the test would be dangerous. A physiologic dose of curare given to a patient with myasthenia gravis would probably be fatal unless artificial respiration was maintained or the antidote prostigmine administered.

SUMMARY

1. It appears that some failure in the action of acetylcholine exists in myasthenia gravis.

2. Physostigmine restores neuromuscular performance in most myasthenic patients.

3. Curare neutralizes acetylcholine action and produces artificial myasthenia gravis.

4. There is some evidence that a primary muscle disorder apart from neuromuscular block may occur in certain stages of the disease.

5. The myasthenic patient exhibits a pronounced sensitivity to curare. One-tenth the usual physiologic dose of curare produces profound exacerbation of existing symptoms, and generalized curarization adds new symptoms of myasthenia.

6. These phenomena suggest a specific diagnostic test for the disease. Injection of one-tenth the usual physiologic dose of standardized curare is a safe procedure if followed by administration of prostigmine methylsulfate. Larger doses must be administered with caution, as fatalities may occur.

7. Five patients with different phases of the myasthenic syndrome have shown a specific response to the curare diagnostic test, even though for some the prostigmine test was inconclusive.

8. The cause of myasthenia gravis should be found by explaining the occurrence in the disease of the neurophysiologic disturbance resembling chronic curarization.

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DISTURBANCES IN PAROTID SECRETION IN AN UNUSUAL NEUROLOGIC SYNDROME

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In this communication we wish to describe a method for measuring the disturbance in parotid secretion in an unusual syndrome involving the artery of the facial nerve—a branch of the anterior inferior cerebellar artery.

In 1901 Wallenberg [1] reported the case of a 70 year old man who had sudden loss of consciousness preceded by a brief period of tinnitus in the right ear and itching of the nose. The period of unconsciousness lasted twenty-four hours; on recovering the patient complained of vertigo. Neurologic examination revealed bilateral involvement of the sensory fifth nerve; paresis of the right motor fifth nerve; paralysis of the right sixth nerve; paralysis of the right seventh nerve, of peripheral type, and partial deafness, right eighth nerve. Pain and temperature sensations were diminished on the left side down to the second dorsal segment. There was slight hyperreflexia on the same side. The clinical diagnosis was hemorrhage from the ramus centralis arteriae radicularis nervi facialis dextri, a branch of the anterior inferior cerebellar artery. The patient lived seven years after his vascular insult. At necropsy the right side of the pons appeared much smaller than the left. Section revealed a hemorrhagic cyst in the tegmentum of the pons extending to the floor of the fourth ventricle. Caudally it reached the anterior end of the inferior olive and rostrally the lingula of the cerebellum. The cyst destroyed the motor nucleus, as well as part of the sensory nucleus and some of the sensory roots of the right fifth nerve. The nuclei of the sixth and seventh nerves on the right side were destroyed, as were the nuclei of Bechterew and Deiters, part of the restiform body, part of the posterior longitudinal bundle, the dorsal fibers of the cochlear nucleus as they passed to the trapezoid body and part of the spinothalamic and spinotectal tracts on the same side.

From the Neuropsychiatric Division of the Montefiore Hospital.

1. Wallenberg, A.: Klinische Beiträge zur Diagnostik akuter Herderkrankungen des verlängerten Markes und der Brücke, Deutsche Ztschr. f. Nervenh. **19**: 227, 1901.

Wallenberg [2] expressed the belief that the extent of the lesion corresponded to the distribution of the branch of the anterior inferior cerebellar artery accompanying the right facial nerve, as was predicted clinically. Our own case resembled clinically the case just described.

REPORT OF A CASE

A white man, aged 46, a house painter for twenty years preceding his illness, had never suffered any symptoms that could be attributed to lead intoxication. The family and past history were noncontributory.

On Dec. 26, 1938, shortly after supper, he complained of a sudden lightning-like pain radiating from the left side of his face and head down the entire left side of the body. He did not lose consciousness but had to be carried to bed. He vomited for several hours thereafter. He felt numb and stiff over the entire left side of the body, although there were no paralyses. During the next few days he noticed that he could not close his right eye and that his mouth was pulled to the left. He also noted difficulty in chewing and speaking and a decided change in the quality of his voice. He experienced considerable dizziness, and a coarse tremor of his left hand, most pronounced on intention, developed. He was taken to a city hospital, where he remained for five months. During this time sensation on the left side of the body improved considerably and there was diminution of the tremor. All other symptoms remained essentially unchanged. Tarsorrhaphy was performed on the right side for iritis and keratoconjunctivitis. Shortly before admission to the Montefiore Hospital he complained of severe pain in one spot inside the left ear. In addition, he became aware of an intermittent whistling noise in the right ear.

Physical Examination.—Examination on admission gave essentially normal results. The blood pressure was 120 systolic and 90 diastolic. There was a tarsorrhaphy scar on the right side. The positive neurologic signs on admission were as follows:

1. A wide-based, conspicuously ataxic gait, with a tendency for the patient to fall in any direction.

2. Bilateral cerebellar signs, most noticeable on the the left, and a tendency to past pointing on the left.

3. Coarse tremor of the outstretched hand, most pronounced on the left and increased on intention.

4. Rhythmic myoclonus of the soft palate, pharynx and larynx, with a rate of 180 per minute.

5. Dysarthric, slurred, high-pitched, explosive speech.

6. Hyperactive tendon reflexes on the left; diminished left abdominal reflexes; no pathologic reflexes.

7. Hypalgesia, hypthermesthesia and hypesthesia over the entire left side of the body and face, with sparing of vibratory and position sensations.

8. Moderate inward deviation of the right eye and loss of lateral conjugate gaze in either direction; normal vertical gaze.

9. Vertical nystagmus on upward gaze.

10. Sluggishness of the left corneal reflex.

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2. Wallenberg, A.: Anatomischer Befund in einem als Blutung in die rechte Brückenhälfte, etc. aus dem Ramus centralis arteria radicularis nervi facialis dextri geschilderten Falle, Deutsche Ztschr. f. Nervenh. **26**:436, 1904.

11. Diminution in superficial sensation over the left side of the face and the anterior wall of the external auditory canal.

12. Complete lower motor neuron paralysis of the right seventh nerve.

13. Bilateral partial nerve deafness, most noticeable on the right.

14. Bilateral absence of labyrinthine response to Bárány test.

15. Bilaterally diminished palatal and pharyngeal reflexes, the responses on the right being more sluggish than those on the left.

16. Questionable weakness of the right motor fifth nerve, and fibrillations of the tongue.

17. Moderate arteriosclerosis of the retinal vessels.

Laboratory Data.—The results of all laboratory studies were within normal limits. The spinal fluid showed an initial pressure of 115 mm. There were 5 lymphocytes per cubic millimeter, and the protein was 37 mg. per hundred cubic centimeters.

Subsequent Course.—In the five months which has elapsed since the patient's admission to the hospital involvement of the right motor fifth nerve has become definite. In addition, myoclonic movements of the diaphragm have been recently observed fluoroscopically. The neurologic status has otherwise remained the same.

It is evident that the involvement of the cranial nerves in our case was practically identical with that observed by Wallenberg in his case. In addition, there were hyperreflexia on the left side and similar sensory dysfunction in the 2 cases. Cerebellar involvement was plainly evident in our case and was probably present in Wallenberg's case, although his description does not make this certain. Inasmuch as the lesion in Wallenberg's case involved the central tegmental tract, palatal myoclonus should have been present, as in our case, although it was not mentioned.

Several investigators have pointed out [3] that the motor secretory nucleus of the parotid gland, the inferior salivatory nucleus, is located in the region covered by the lesion observed in Wallenberg's case. Inasmuch as we felt that the lesion in our case closely resembled in its anatomic relation that observed in Wallenberg's case, a disturbance in parotid secretion on the right side was anticipated.[4] Studies of parotid secretion on this patient were accordingly begun.

STUDY ON PAROTID SECRETION

Method.—Measurements of parotid flow were made by the Strongin parotid secretory disk.[5] This instrument consists of two metal cups, one soldered within

3. Kohnstamm, O., and Wolfstein, D. J.: Versuch einer physiologischen Anatomie des Vagusursprung und des Kopfsympatheticus, J. f. Psychol. u. Neurol. **8**:177, 1907. Yagita, K., and Hyama, S.: Ueber das Speichelsekretioncentrum, Neurol. Centralbl. **28**:738, 1909. Feiling, A.: On the Bulbar Nuclei with Reference to the Existence of a Salivatory Center in Man, Brain **36**:255, 1913.

4. Dr. Otto Marburg suggested the possibility of such a condition and guided us in the preparation of this report.

5. Dr. E. Strongin gave us the use of his disks and his technical advice. The actual disk is about the size of a dime.

the other. The disk is placed over the papilla of Stensen's duct so that the papilla lies entirely within the inner cup. With a little practice and with good lighting this is easily performed. The disk is held in position against the buccal mucosa with one hand. The operator then makes suction on tube *B*. This creates a vacuum in the space between the inner cup (*C*) and the outer cup (*A*), which secures the disk in its proper position. A small pinch clamp is then placed on tube *B*. Relatively little suction on tube *B* is necessary to produce the required vacuum. Under no circumstances should the subject experience pain or discomfort due to the suction. The pinch clamp can then be secured to the subject's clothing by means of a safety pin. The outlet from the inner cup is connected with a 1 cm. pipet (*D*) calibrated in hundredths of a cubic centimeter. The length of the tubing used in establishing this connection does not matter. Before the connection is made a droplet of water is placed within the pipet. It is the movement of this droplet that is recorded.

It is desirable to conduct these measurements in a soundproof room, since extraneous stimuli may produce alterations in the parotid flow. It is preferable that the subject have had no medication for the preceding forty-eight hours. Studies should be made in the morning. The subject omits breakfast and is not permitted to smoke. The procedure is explained to him in simple terms, and every effort is

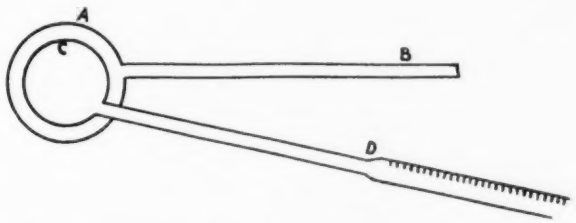

Diagram of the Strongin parotid secretory disk.

made to set him at his ease. He is instructed to sit back comfortably in his chair with his eyes open. He should not fall asleep during the experiment and should not read or engage in other mental activity.

When the disk is properly placed, movement of the water droplet in the pipet is almost immediately evident. (There may be a latent interval of psychic inhibition of parotid secretion, lasting several minutes.) The position of the disk can be rapidly checked by putting a drop of lemon juice on the subject's tongue. This procedure will be followed by an almost instantaneous spurt of the water droplet. A dropper bottle containing lemon juice is made available for this purpose. After this procedure at least six minutes must elapse before measurements are made. They are carried out as follows: The subject is instructed to swallow once and then to swallow no more until told to do so. In the event that he swallows before he is instructed to do so, he must signify this fact by raising his hand. Measurements must then be started all over again, beginning with this swallow. The flow during the first minute following the swallow is discarded. Readings of the position of the droplet are then made every minute for five minutes, at which time the patient is ordered to swallow. The procedure is then repeated. For most accurate determination of the resting secretory rate six such intervals should be recorded. The pipet must be chemically clean and perfectly dry.

Results.—The resting secretory rates recorded on Feb. 27, 1942 follow.

	Readings, Cc.	
	Left	Right
	0.930	0.910
	0.855	0.905
	0.812	0.901
	0.732	0.900
	0.680	0.895
	0.600	0.889
Total secretion	0.33	0.02
	0.535	0.886
	0.482	0.884
	0.425	0.882
	0.350	0.875
	0.302	0.873
	0.255	0.871
Total secretion	0.28	0.02
	0.960	0.869
	0.900	0.867
	0.855	0.862
	0.790	0.859
	0.735	0.852
	0.680	0.850
Total secretion	0.28	0.02

Stimulation with lemon juice produced spurts of parotid secretion on the left side, but not on the right, even when the right side of the tongue was stimulated directly. (Ordinarily, stimulation of the right side of the tongue produces a primarily ipsilateral parotid response, and vice versa.)

On injection of $\frac{1}{80}$ grain (8 mg.) of pilocarpine hydrochloride hypodermically the following results were obtained:

	Readings, Cc.	
	Left	Right
	0.860	0.845
	0.810	0.842
	0.730	0.841
	0.625	0.835
	0.555	0.830
	0.470	0.820
Total secretion	0.49	0.02

	Readings, Cc.—*Cont.*	
	Left	Right
	0.370	0.807
	0.300	0.788
	0.230	0.765
	0.150	0.730
	0.070	0.690
	0.010	0.640
Total secretion	0.36	0.17
	0.920	0.575
	0.800	0.500
	0.710	0.425
	0.600	0.350
	0.480	0.268
	0.375	0.185
Total secretion	0.55	0.39
	0.940	0.812
	0.820	0.732
	0.625	0.662
	0.500	0.580
	0.350	0.510
	0.200	0.435
Total secretion	0.74	0.38

It should be noted that the increase in secretion on the right side set in six minutes after the injection of pilocarpine. This time interval was noted by Strongin [6] in a large series of cases of non-neurologic conditions with a high degree of regularity. There seemed to be somewhat of a lag in the response to pilocarpine on the left side. However, at the termination of the experiment the left side again far outstripped the right in rate of secretion.

Repetition of the experiment on May 28 gave the following results:

	Readings, Cc.	
	Left	Right
	0.900	0.810
	0.800	0.810
	0.660	0.810
	0.540	0.810
	0.410	0.810
	0.300	0.810
Total secretion	0.60	0.00

6. Personal communication to the authors.

When lemon juice was placed on the tongue the response was as follows:

	Readings, Cc.	
	Left	Right
	0.900	0.772
	0.790	0.772
	0.650	0.772
	0.480	0.772
	0.370	0.772
	0.260	0.772
Total secretion	0.64	0.00

It should be noted that on this day there was total absence of secretion on the right, which was associated with a much higher rate of resting secretion on the left than was observed in the previous experiment. It should also be noted that there was once more no response to lemon juice on the right. That this was not an artefact due to improper placement of the disk is clear from the following figures, obtained after the injection of $\frac{1}{40}$ grain (16 mg.) of pilocarpine hydrochloride. It should be emphasized that there was no alteration in the position of the disk during this experiment.

	Readings, Cc.	
	Left	Right
	0.980	0.755
	0.890	0.755
	0.800	0.715
	0.540	0.480
	0.400	0.190
Total secretion	0.58	0.57

Although further measurements were not recorded, it can be stated that a profuse parotid flow was observed bilaterally in response to pilocarpine. This proves that the previously noted absence of resting secretion and absence of response to lemon were not artefacts.

COMMENT

It is to be observed that the left parotid gland maintained a resting secretory rate which was considerably higher than that on the right; that whereas the left parotid gland responded to both lemon and pilocarpine, the right gland responded only to pilocarpine. It would seem, then, that since the reflex between the taste buds and the parotid gland was destroyed on the right side, pilocarpine acts directly on the parotid gland. Our results also seem to indicate that the motor nerves of the parotid gland do not have bilateral representation in the brain stem, as was suggested by Kohnstamm on the basis of animal experimentation. The mechanism of the compensatory increase in secretion on the side opposite the lesion is speculative. It is possible that this

increase represents a release phenomenon due to the destruction of contralateral supranuclear autonomic pathways. The anticipated hypersensitivity of the denervated right parotid gland to pilocarpine, in accordance with Cannon's law of denervation, was not observed.

The Strongin technic thus afforded a precise method for demonstrating the anticipated disturbance in parotid secretion in this patient. It permitted the elucidation of the nature of this disturbance and the nature of the action of the pilocarpine on parotid secretion. The method is presented in detail in the belief that it provides a useful tool in conducting a clinical neurologic examination, which may be as valuable in other cases at it proved to be in ours.

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TREATMENT OF POST-LUMBAR-PUNCTURE HEADACHE WITH ERGOTAMINE TARTRATE

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The object of this paper is to summarize some observations on the treatment of post-lumbar-puncture headache, following spinal anesthesia, with ergotamine tartrate.

The use of ergotamine tartrate for the treatment of post-lumbar-puncture headache was mentioned by Targowla and Lamache.[1] They reported that ergotamine tartrate seemed to be of value in the treatment of post-lumbar-puncture phenomena. Lennox, von Storch and Solomon[2] reported on the effect of ergotamine tartrate on nonmigrainous headache. In their series of patients who were unsuccessfully treated for many types of headache other than migraine were 7 who had headaches and a decreased cerebrospinal fluid pressure after lumbar puncture.

PRESENT INVESTIGATIONS

The 35 patients who were treated with ergotamine tartrate were from a group of 418 patients on whom lumbar puncture was performed and spinal anesthesia induced (with procaine). Most of the patients who received the drug were not allowed out of bed because of some recent operative procedure. They were permitted to remain in any position in bed directly after receiving the ergotamine tartrate. All the patients elected to lie flat in bed. After varying lengths of time following the administration of the drug—from five minutes to two hours—they were allowed to sit up with the head of the bed elevated 50 degrees or more. The effect of having the head of the bed raised was observed and recorded for each patient. The approximate elevation, in degrees, and the time of onset and the character of the symptoms were noted. These data served as a base line for determining the effect of ergotamine tartrate. Some patients, those who received the drug by vein, had the head of the bed raised as often as every five to ten minutes in order that the effect of the drug might be determined.

It is not possible to demonstrate conclusively that headache following the induction of spinal anesthesia is totally independent of the anesthetic agent used, but

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From the Jewish Hospital, Philadelphia.

Ergotamine tartrate (gynergen) was supplied by Sandoz Chemical Works, Inc., New York.

1. Targowla, R., and Lamache, A.: Les accidents de la ponction lombaire et leur traitement, Ann. de méd. **22**:345, 1927.

2. Lennox, W. G.; von Storch, T. J. C., and Solomon, P.: The Effect of Ergotamine Tartrate on Non-Migrainous Headaches, Am. J. M. Sc. **192**:57, 1936.

clinical observations do not indicate any difference in signs or symptoms and this type of headache seems to be identical with the post-lumbar-puncture headache.

Ergotamine tartrate (gynergen) was given to 35 patients who had post-lumbar-puncture headache following spinal anesthesia.

Ergotamine tartrate is a potent drug. The dose is that amount which is sufficient to produce the desired effect in a particular patient. One patient may be able to tolerate as much as 1 mg. given parenterally within several hours and show no minor toxic symptoms, while another may exhibit toxic phenomena after receiving 0.25 mg. The drug was usually administered parenterally—frequently by vein, usually by deep subcutaneous or muscular injection. In some instances the drug was administered sublingually.

For parenteral administration the following method was found to be fairly satisfactory. The patient was given from 0.25 to 0.50 mg. of ergotamine tartrate into the deltoid region. One of several things occurred during the next two hours.

Effect of Ergotamine Tartrate on Post-Lumbar-Puncture Headache

	No. of Patients	Percentage
Patients treated	35	100.0
Result of treatment		
Relief	29	82.9
Some relief	2	5.7
No relief	4	11.4

1. The patient was able to sit up or walk about, if ambulatory, free of a headache or with but a very slight ache. For about two to three tenths of the patients one dose was sufficient and the headache did not return. It is now deemed advisable to give a patient the same dose two or three times a day for about two days to ward off any recurrence. When the headache was relieved and then returned, the recurrence was from four to twelve hours after the drug was administered.

2. The patient was relieved and could be up without a headache, but some of the minor toxic symptoms, e. g., loss of appetite, nausea, vomiting and various vasospastic phenomena, occurred. The patient responded favorably to the drug, but the therapeutic dose had been exceeded. Subsequent doses for such patients should be between one-half to two-thirds the initial dose, so that minor toxic symptoms do not recur.

3. The patient was not improved, and no minor toxic symptoms appeared. When this occurred, either a therapeutic dose had been administered and the patient did not obtain relief from the drug or a therapeutic dose had not been given. To these patients a 0.25 mg. dose was administered every two to three hours until he was able to be up

without a headache or there was no change in the intensity of the headache and minor toxic symptoms appeared. The drug is not supposed to be given in excess of 1 mg. (parenterally) in twenty-four hours. However, it has been noted that some patients can be given as much as 2 mg. in twenty-four hours for several days without the appearance of minor toxic symptoms. In general 1 mg. should be the maximum amount for twenty-four hours.

4. The patient exhibited minor toxic symptoms with no relief from the headache. The dose was repeated in twelve hours, and if the same result occurred it was deemed that the patient derived no benefit from ergotamine tartrate.

Ergotamine tartrate was administered by the intravenous route to 8 patients. Each person received 1 cc. of physiologic solution of sodium chloride by vein about two hours before ergotamine tartrate was administered, and in no instance was relief afforded by the injection of the saline solution. After injection of 0.25-0.50 mg. of ergotamine tartrate by vein the patients reported beginning relief from the headache in fifteen to thirty minutes. These patients were usually made to sit up each five to ten minutes, and by the end of a half-hour the headache was entirely gone or greatly diminished in intensity. This method was employed to demonstrate the precise response to intravenous administration, and it may be used in treating patients with severe headache or as a final measure in attempting to treat that group who do not seem to respond to ergotamine tartrate.

Ergotamine tartrate, at least according to these data, is of value in relieving post-lumbar-puncture headache in eight to nine tenths of the patients only when the drug is administered according to the tolerance of the particular patient for the drug. Each person differs in this respect, and one must administer the drug as carefully as one rapidly digitalizes a patient or as one administers morphine sulfate to a patient with acute myocardial infarction. The dose for a particular patient is that amount of the drug which gives the desired therapeutic effect. Once the dose for a patient is determined it is advisable and practical to employ this quantity or to reduce it to the minimal therapeutic dose.

710 West One Hundred and Sixty-Eighth Street.

JUVENILE AMAUROTIC IDIOCY

A CLINICOPATHOLOGIC STUDY

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Clinicopathologic studies of the juvenile type of amaurotic family idiocy are infrequent. The present case offers an opportunity to correlate the neurologic, psychologic and electroencephalographic studies made shortly before the patient's death with the pathologic observations.

REPORT OF A CASE

A 16 year old youth entered the hospital Nov. 1, 1940 with the complaint of blindness for ten years, loss of memory and convulsions for one year. His development was said to have been normal until he was 6 years old. There was no family history of any neurologic or psychiatric disorder. His mother, father and 20 year old brother were alive and well.

At the age of 6 years his mother noticed that he started to bump into objects, and soon after beginning school his first grade teacher noted difficulties in vision. An ophthalmologist told the parents that the condition would progress to complete blindness. During the following two years he lost all vision in both eyes save light perception. He was enrolled in a school for the blind when he was 8 years old. He disliked the school, was resentful of his blindness and failed to learn to read Braille. From the age of 11 to 15 years he was kept in a private school; he is said to have done satisfactory school work and to have become socially adjusted. In October 1939 he began to have convulsive seizures of the grand mal type; at first they occurred once or twice each week but subsequently increased in frequency to once every two or three days. They sometimes occurred in groups with repeated seizures during a single day.

Physical Examination.—Nothing abnormal was noted except in the neurologic and ophthalmoscopic examinations. His gait was moderately ataxic. The Romberg sign was positive. There was some dysmetria in all extremities. All of his movements were rather slow. There was generalized hypotonia, though he was not particularly weak. An occasional choreiform movement was noted. Of the deep reflexes of the upper extremity only the left biceps was elicitable, and it was weak. The knee jerks were difficult to obtain, but the ankle jerks were brisk. The abdominal reflexes were sluggish. The big toes were maintained in a con-

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stant state of dorsiflexion; no pathologic reflexes were elicited. All types of superficial and deep sensation were intact. Only light perception was present in both eyes. The optic disks were flat and yellowish; all retinal vessels were extremely narrow. Small spicules of pigment were scattered over the entire surface of the fundus, only a few being present, however, at the macular area or around the disk. Both lateral and vertical nystagmus were present and were greatly accentuated after the air encephalogram was taken. No evidence of involvement of other cranial nerves was noted.

Mental Examination.—The boy was ordinarily cooperative, although he had an occasional temper tantrum. His mood was rather indifferent. He spoke volubly. Sometimes, however, he merely repeated "yes" over and over again, explaining that the nurses were asking him whether he could see. There was no other evidence of hallucinations or delusions. He knew the date of the month but was unable to state where he was or to give the name of the president. His memory was poor, and his judgment was greatly impaired. The psychometric report by Dr. Ann Magaret follows:

"Classification: The patient is mentally deficient (probably an imbecile).

"Test Results: The revised Stanford-Binet test form L gave a mental age between 6 and 7 years. The average grade level with the Lowe-Shimberg scaled information test was below the fourth, probably at the second. The average mental age was below 9 years, probably 6 years.

"Analysis of Test Results: Interpretation of these results should be made with caution, since Donald is blind and could be given only such verbal tests as could be presented orally. None of the concrete performance tests was applicable. His general vocabulary on the Stanford-Binet list is at the 8 year level. On tests of immediate memory he falls at the 5 year level, and on tests of general comprehension, at the 8 year level. His fund of general information is that which would be expected from a second grade pupil. His ability to succeed with some information items at recognition, when he had failed to recall them, suggests that he may have known many of the questions at some time in the past, although he is today unable to answer them.

"Comment: Donald is a hesitant, uncertain but friendly and cooperative boy, who seems to exert a tremendous amount of effort in the test situation. He is cheerful and talkative, asks numerous questions about the materials used for the test and volunteers much information about the schools he has attended and the doctors he has seen.

"His attack on the test items is delayed and somewhat erratic. Frequently he succeeds with numerous subtests on a given item, only to fail on the crucial one, and hence lose all credit. He gives the impression of having to search long for his answers; his responses are slow, poorly phrased and uncertain. He stutters markedly when he is blocked on a question and always gropes for the proper words to express his answers. Nevertheless, he seems able to maintain his attention for unusually long periods. He seldom asks for repetition of instruction. He is often blocked in recalling names of simple objects; he struggled long to remember the word 'grass,' and finally asked in desperation, 'What do you call that stuff in the back yard?'

"Impression: The general impression is that of a cheerful, friendly, cooperative but hesitant and uncertain boy of imbecile grade intelligence. The wide discrepancy between his performance on vocabulary and on immediate memory items; his blockings on many of the questions; his ability to succeed with items on a recognition level when he has failed to recall them, and his general delay

and retardation in his test behavior, all are in agreement with the diagnosis of mental deterioration, which seems unquestionable in view of the earlier test results (intelligence quotient 133 at the age of 3 to 6 years)."

Laboratory Data.—The blood count and urinalysis revealed nothing abnormal. The sedimentation rate was 8 mm. per hour. The spinal fluid was normal: The Pandy reaction was negative, the total protein 22 mg. per hundred cubic centimeters and the colloidal gold curve 1112100000. The Wassermann reaction was negative for both the blood and the spinal fluid. The spinal fluid pressure was elevated, being over 300 mm. of water with the patient in a horizontal position. Flat roentgenograms of the skull were normal.

Electroencephalogram: Eight to 9 per second waves were revealed in all areas (Nov. 2, 1940). A small amount of random slow activity was present, being greatest in the occipital leads (fig. 1). None of this slow activity was of great amplitude, the maximum being 50 microvolts.

Air Encephalogram: On November 4, Dr. R. R. Newell reported: "The ventricular system is of rather large volume (fig. 2). In the left temporo-occipital region there is a superficial channel which seems somewhat increased in size. There are a few channels on the mesial surfaces of the hemispheres, but elsewhere the subarachnoid channels are scanty or wanting."

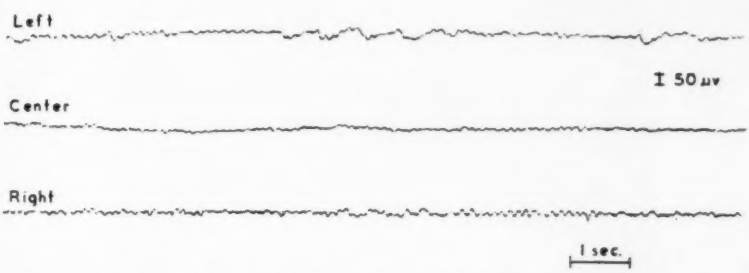

Fig. 1.—Electroencephalogram from the occipital region. Some slow random waves of low amplitude are present on the left side. The alpha rhythm is usually 8 to 9 per second.

Course.—A diagnosis of amaurotic family idiocy of the juvenile type was made. The patient was admitted to the Napa State Hospital, Imola, Calif., on November 26. A report from there stated that he was agreeable, childish, asked many questions, but wanted to go home. He ate and slept well. His speech remained relevant and coherent until his terminal pneumonia. He died Jan. 6, 1941. Dr. I. E. Charlesworth, the medical superintendent of Napa State Hospital, permitted us to examine the brain.

Macroscopic Examination.—The brain appeared to be larger than normal; it weighed 1,450 Gm. The sulci were shallow.

Microscopic Examination.—The characteristic cellular changes of amaurotic family idiocy were observed in the vast majority of the ganglion cells that were examined. These changes were most evident in the cerebral cortex and least so in the caudal end of the medulla. Most of the cells were swollen and appeared to be ballooned or saclike (fig. 3). The Nissl substance had more or less disappeared; it was rarely seen in the cortex. Neurofibrils were not definitely observed in many of the cells stained by the Bielschowsky or the Bodian method; in others

the neurofibrils were pushed to the periphery, sometimes causing the cell wall to appear thickened (fig. 3 *C*). The nucleus was usually at the periphery of the cell or in the base of one of the dendrites (fig. 3 *B*). Its wall was often hyperchromatic. Occasionally it appeared to have burst, and its contents lay free in the cytoplasm. The cytoplasm was usually filled with granules. In sections stained with cresyl violet

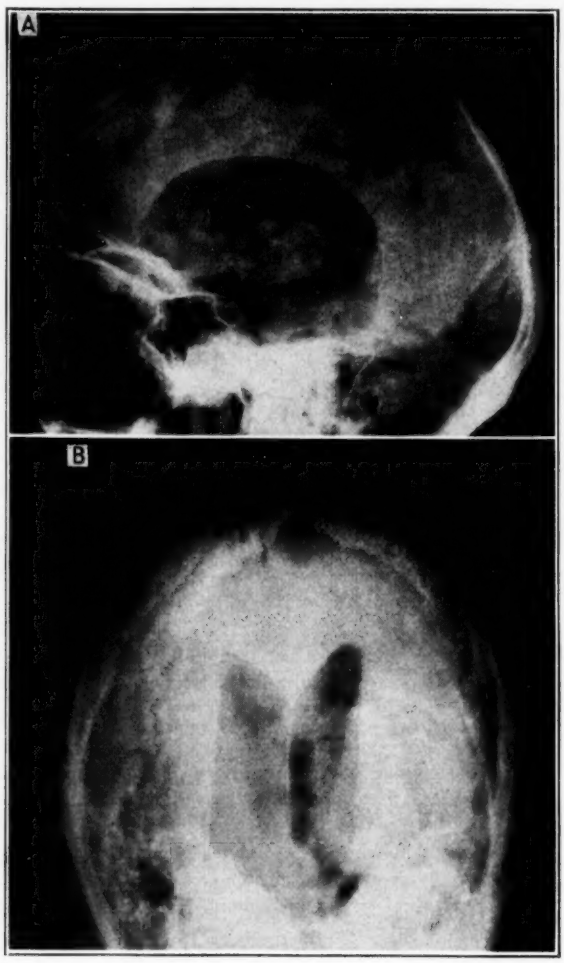

Fig. 2.—Air encephalogram. Except for a rather large superficial channel on the left and a few other channels at the mesial surface, no air has entered the subarachnoid space.

these granules were yellow. With scarlet red they were either yellow or yellow-orange; no bright red granules were observed with this method. Hematoxylinophilic granules appeared in only a few cells in sections stained with the Schaffer method. Mingled with the large cells were some that were smaller and appar-

ently shrunken. Others appeared to be shadow forms, with absence of nuclei and pale pigment. There was disappearance of cells, especially in the cortex; a resultant area of status spongiosus was occasionally seen.

Sections from the frontal lobe, including the frontal pole, the motor area, the premotor area and the gyrus rectus, showed pronounced diminution in the number of cells in all layers, especially in the third and fifth (figs. 4 and 5).

In the first, second and third temporal convolutions and in Heschl's convolution diminution in the number of cells was not as marked as in the frontal region, in spite of severe alterations in individual ones (fig. 6). Cell-free patches, how-

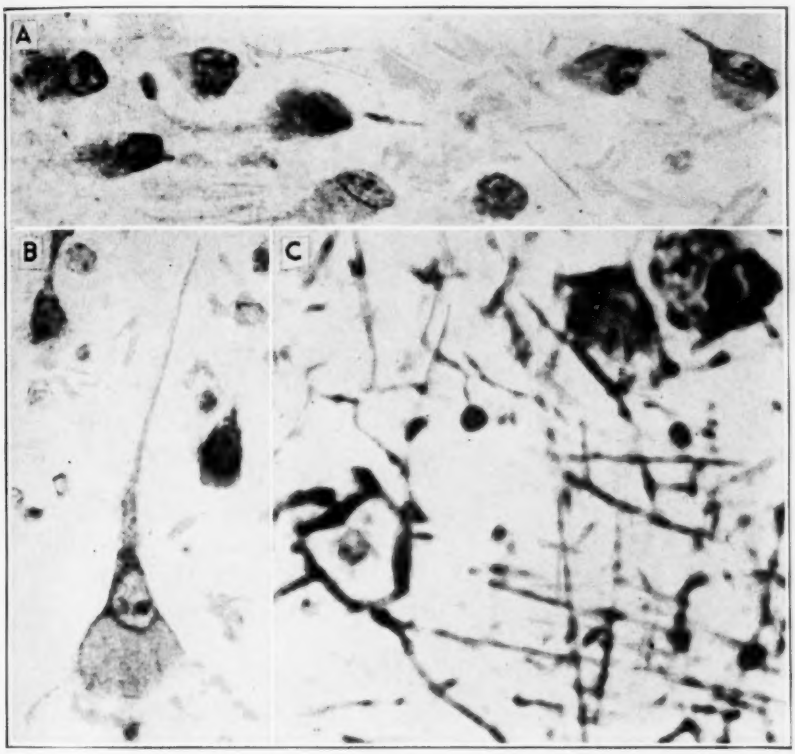

Fig. 3.—*A*, swollen spindle cells in the sixth layer of the cortex. Cresyl violet stain. *B*, pear-shaped cell in the lower portion of the third layer. The nucleus is pushed into the apical dendrite. The cytoplasm is filled with pigment. Cresyl violet stain. *C*, ballooned cells in the fifth layer. The nuclei and neurofibrils are at the periphery. Bodian stain.

ever, were present and were most evident in the third layer. Loss of cells in all layers was also noted in the posterior central gyrus, the superior parietal lobe, the supramarginal gyrus and the angular gyrus of the parietal lobe (fig. 7). Similar to that in the temporal region, this loss was not as great as in the frontal lobe. The number of cells was almost normal in the gyrus cinguli. There was no decrease in the number of cells in the gyrus hippocampi and the cornu ammonis.

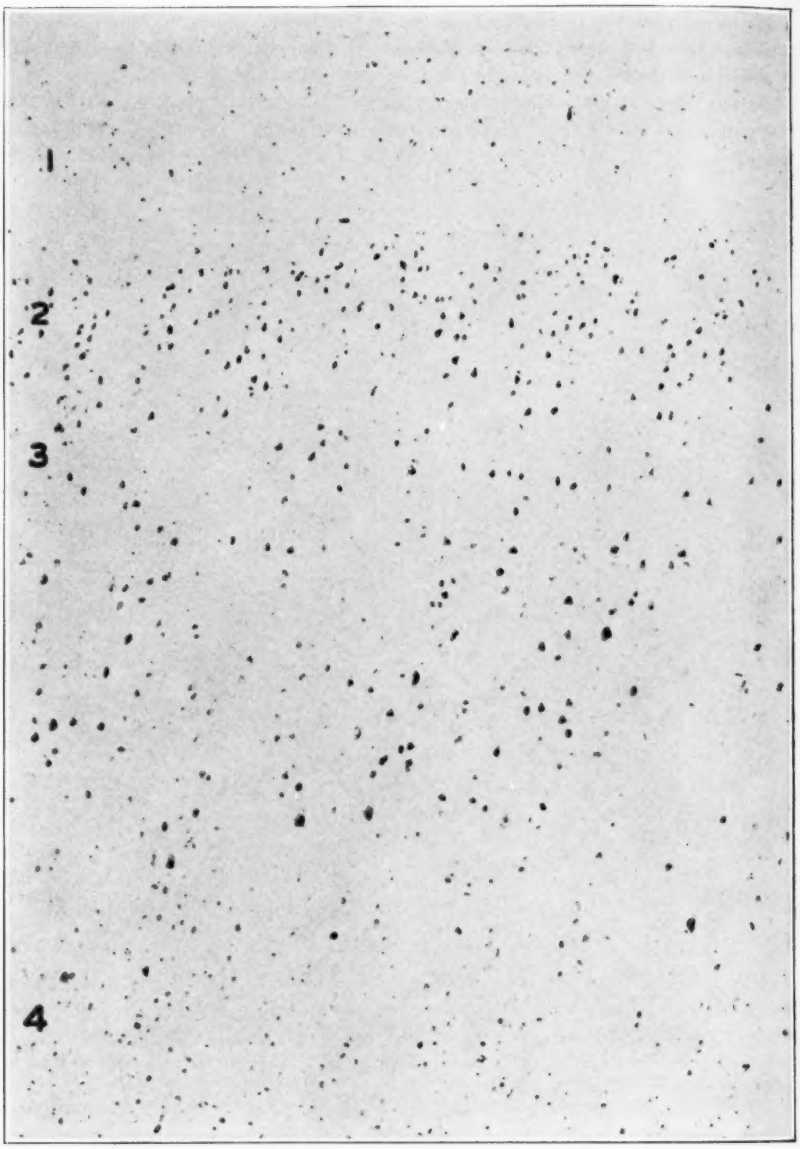

Fig. 4.—Frontopolar region. Many cell gaps are present, especially in the third layer. Cresyl violet stain.

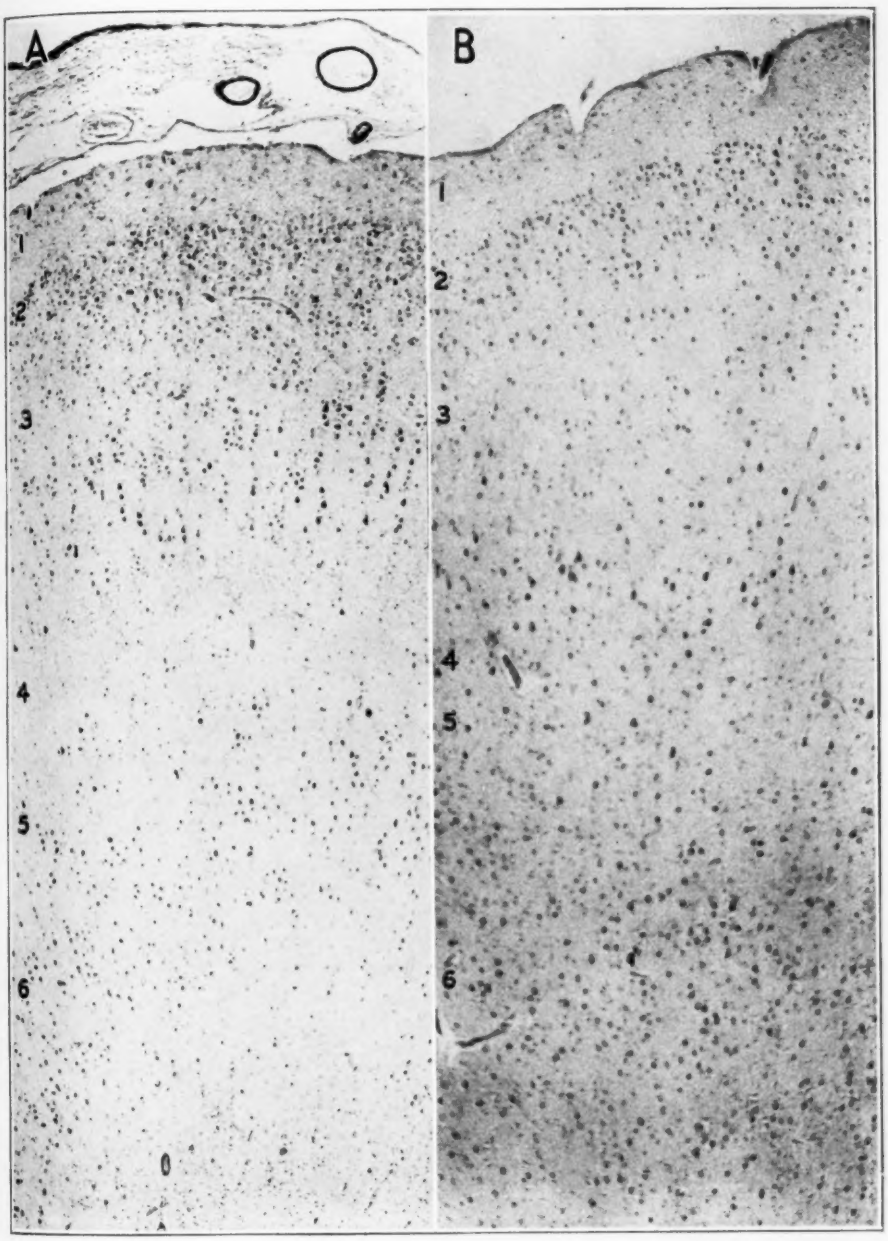

Fig. 5.—*A*, middle occipital gyrus; *B*, superior part of motor area, frontal lobe. Loss of cells is much more pronounced in the frontal than in the occipital lobe. The giant pyramidal cells are absent. The pia-arachnoid in *A* is thickened and contains many histiocytes. Cresyl violet stain.

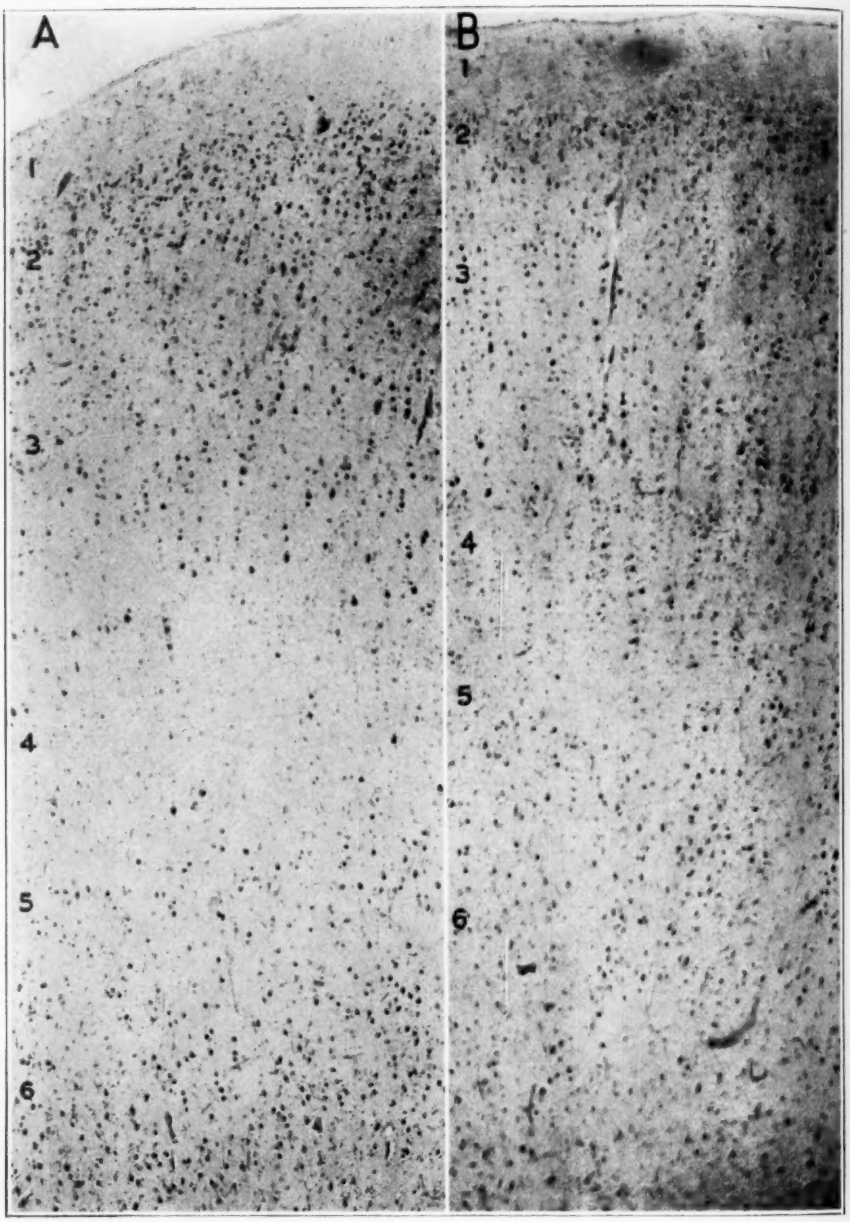

Fig. 6.—*A*, second, and, *B*, third temporal gyrus. Cellfree patches are especially evident in the third and fifth layers. Cresyl violet stain.

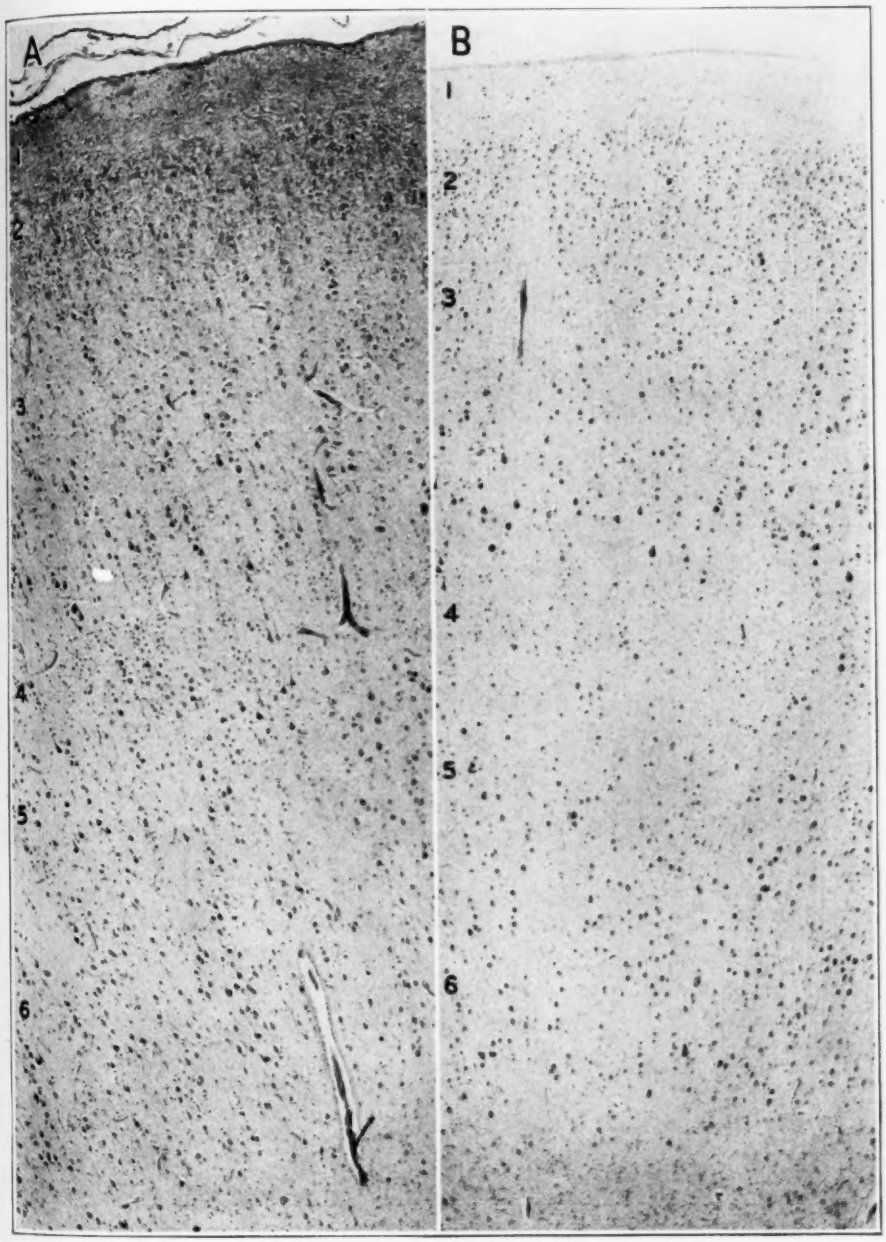

Fig. 7.—*A*, supramarginal gyrus; *B*, superior parietal lobe. The cell loss is similar to that in the temporal lobe.

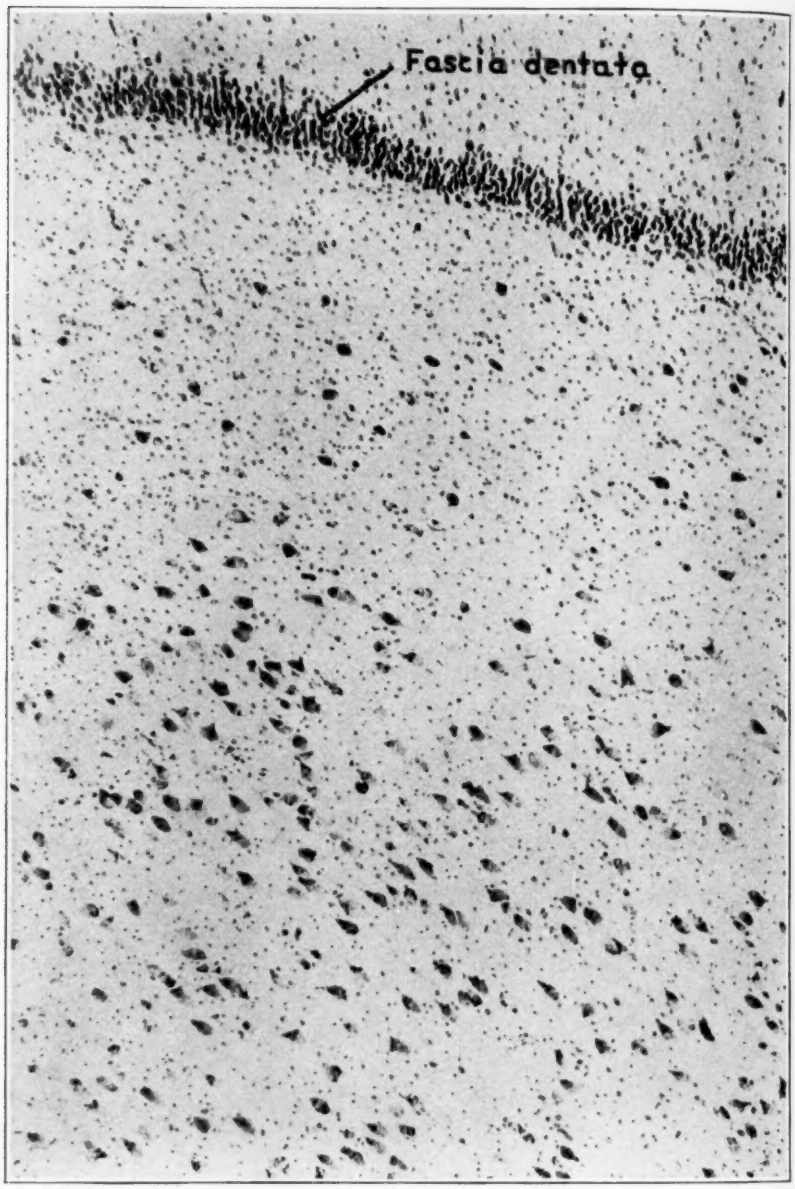

Fig. 8.—Cornu ammonis. All of the large cells are swollen; those in the fascia dentata are of normal size. Cresyl violet stain.

However, all of the large cells of the cornu ammonis were affected. Most of the smaller ones in the fascia dentata appeared to be normal (fig. 8). In the subiculum some of the cells were normal in both shape and size. Sections from the occipital lobe, including the area striata and the medial and superior occipital gyri, appeared to have the least diminution in the number of cells (fig. 5); in fact, the number sometimes appeared to be normal. The molecular layer contained numerous swollen astrocytes in all parts of the cortex that were examined. Horizontal cells of Cajal were occasionally seen in this layer; they seemed to be degenerating. The radial fibers and the bands of Baillarger were present in all areas examined. The superficial tangential plexus was absent. The number of fibers in the interradiate and superradiate networks was also diminished. This diminution was least prominent in the occipital lobe. Swelling of the glia cells similar to that seen in the ganglion cells was frequently observed. Granules were seen in their cytoplasm, and occasionally the nucleus was homogeneous or degenerated. Neuronophagia was noted occasionally.

Similar types of cell degeneration were observed in the basal ganglia, midbrain, pons, medulla and cerebellum. The lower portion of the medulla appeared to be relatively least affected; some of the large ganglion cells retained their normal appearance and distribution of Nissl substance. No demyelination was present in Pal-Weigert sections. In the cerebellum, most of the Purkinje cells were absent. Those remaining were swollen. Bergmann's glia cells were increased in number. Many of the cells in the granular layer were pale and swollen; some contained vacuoles. The spinal cord was not examined.

The pia-arachnoid was thicker than usual (fig. 5 *A*). There was an increase in the number of fibroblasts, and many of them were swollen. Histiocytes containing granules were also observed.

COMMENT

The disorder in this case was typical of the juvenile form of amaurotic family idiocy from both the clinical and the pathologic aspect. The photographic similarity among cases mentioned by Sjögren[1] was present, namely: (1) initial onset of visual disturbances between the fifth and the eighth year, progressing to total blindness in one or two years, with retinitis pigmentosa and optic nerve atrophy; (2) mental deterioration and behavior disturbances, progressing throughout the course of the disease; (3) convulsions, usually beginning fairly late; (4) other neurologic manifestations, such as ataxia, tremors, nystagmus and pathologic reflexes, usually appearing during the terminal phase, and (5) death occurring from ten to fifteen years after the onset.

The histologic alterations were also characteristic and resembled those described in the more common, infantile form of the disease. Widespread alterations in cell structure were present throughout the brain. These consisted mainly of balloon-like swelling and deformation, with deposition of lipoids in the cytoplasm. Other cells might be shrunken or missing. The nucleus was pushed to the periphery or into

1. Sjögren, T.: Die juvenile amaurotische Idiotie: Klinische und erblichkeitsmedizinische Untersuchungen, Hereditas **14**:197, 1931.

the base of the dendrites. The latter were frequently swollen or corkscrew. The structure of the nucleus was better preserved than that of the cytoplasm, though its wall might be hyperchromatic or even destroyed. Nissl substance was usually absent; it was rarely seen in the pyramidal cells of the cortex. In many of these cells the neurofibrils were completely replaced by lipoidal granules. In others a few neurofibrils might be seen adjacent to the cell wall.

Although some writers have expressed the opinion that granules consisting of neutral fat are characteristically seen in the juvenile form, in contrast to the prelipoids of the infantile form, this did not appear to be true in the present case, as the granules did not stain red with scarlet red.

Changes were present in all of the numerous cortical areas that were examined, in general decreasing in severity from the frontal to the occipital region. The pyramidal cells of the third and fifth layers showed the most striking alterations. Few of the cells retained their normal contour. A decrease in the number of cells was apparent, and numerous gaps were observed. No giant pyramidal cells were observed in the motor area. None of the other cortical laminas escaped involvement, however. The molecular layer appeared sclerotic; numerous swollen astrocytes were noted. The superficial tangential plexus was absent. A few degenerating horizontal cells of Cajal were seen in this layer. Ostertag [2] noted them in the infantile form. These cells, which ordinarily disappear completely after birth, have been said to be a sign of arrested development.[3] Alterations of the small pyramidal cells in the second layer were more difficult to detect than those in the third or fifth layers but were nevertheless, definite. Some of these cells were swollen, but most had only a fragment of cytoplasm adjacent to the nucleus. Regardless of its amount, the cytoplasm was filled with granules of the same type as those seen in the larger pyramidal cells. Ostertag observed only shrunken cells in the second layer, in contrast to the swollen ones seen elsewhere. He therefore made the assumption that there were two different types of degeneration. The evidence in the present case indicates that the small, lipoid-containing cells may represent either a stage preceding swelling or subsequent shrinkage, similar to that seen in axonal degeneration. Most of the star cells in the fourth layer were swollen and filled with lipoid. Many of the spindle cells of the

2. Ostertag, R.: Entwicklungsstörungen des Gehirns und zur Histologie und Pathogenese besonders der degenerativen Markerkrankung bei amaurotischer Idiotie, Arch. f. Psychiat. **75**:355-391, 1925.

3. Gerstmann, J.: Beitrag zur Kenntnis der Entwicklungsstörungen in der Hirnrinde bei genuiner Epilepsie, Idiotie, juveniler Paralyse und Dementia praecox, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **21**:286-313, 1916.

sixth layer had lost their normal contour and become rounded. The radial fibers and the bands of Baillarger were present in all regions of the cortex, while the tangential fibers and the superradiate and interradiate networks had partially disappeared. Diminution of the number of cells was not present in the region of the cornu ammonis, although swelling and lipoidosis were particularly striking in the larger ones. Many cells in the subiculum were normal in size and shape. This picture is in contrast to Scherer's [4] description of a decrease in cells in the dorsal foliage of the cornu ammonis and its transition into the fascia dentata, while the cells of Sommer's sector remained comparatively intact.

Similar widespread alterations in structure have been reported by other investigators in various areas of the cortex in cases of the juvenile form of amaurotic idiocy. Their observations usually differ only in the relative intensity of the process in the different areas and layers. Schob,[5] for instance, was unable to recognize any normal cells in the cortex. Globus [6] also described a universal distribution of the lipoidosis in the cortex in his case. He stated that the third and fifth layers were especially affected, but that portions of the fourth layer were seriously involved in the area striata. Status spongiosus was present where the cells had disappeared. Greenfield and Holmes [7] encountered no distinction in the degree of cell change in various regions except that some cells in the hippocampus were more diffusely swollen than any others in the cortex. They observed that the diminution in number of cells affected all layers indiscriminately. Taft and Monroe's [8] case of the juvenile type was characterized by severe degeneration in the calcarine area and relative intactness in the hippocampal region; all layers were affected. In Hassin's [9] case of the late infantile type the third, fourth and fifth layers of the occipital lobe were practically destroyed and replaced by neuroglia. In our case the cytoarchitecture was especially well preserved in this region. Involvement of all the

4. Scherer, H. J.: Die Ammonshornveränderungen bei der familiären amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:481-492, 1932.

5. Schob, F.: Zur pathologischen Anatomie der juvenilen Form der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:303-324, 1912.

6. Globus, J. H.: Ein Beitrag zur Histopathologie der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:424-466, 1923.

7. Greenfield, J. G., and Holmes, G.: The Histology of Juvenile Amaurotic Idiocy, Brain **48**:183-217, 1925.

8. Taft, A. E., and Monroe, J. P.: Familial Preadolescent Mental Deterioration and Blindness, Am. J. Psychiat. **5**:87-92, 1925.

9. Hassin, G. B.: A Case of Amaurotic Family Idiocy, Late Infantile Type (Bielschowsky) with Clinical Picture of Decerebrate Rigidity, Arch. Neurol. & Psychiat. **16**:708-727 (Dec.) 1926.

layers in all cortical areas was also described by Dide and van Bogaert,[10] although they expressed the belief that the deeper layers were more severely damaged.

It may be concluded that cortical alterations consist mainly of (1) diffuse lipoidosis and swelling of ganglion cells; (2) completely asystematic, patchlike disappearance of cells, most striking in the third and fifth layers, and (3) sclerosis of the molecular layer with loss of tangential fibers.

It is remarkable that in spite of involvement of the vast majority of cortical cells the loss of function was not greater. While considerable mental deterioration had occurred, the patient nevertheless was cooperative and talkative; in tests of vocabulary and general comprehension he was at the 8 year level. As in most cases of the juvenile type of amaurotic idiocy, no sensory or auditory impairment was observed. No aphasia, agnosia or apraxia was present. Taft and Monroe [8] stated: "The loss of vision is usually due to cortical degeneration, in contrast to the macular change and optic atrophy which is found in the infantile group." This appears to be unlikely in the present case. Not only was the calcarine area relatively less damaged than other portions of the cortex, but severe degenerative changes (retinitis pigmentosa with optic nerve atrophy) were present in the fundus.

The electroencephalographic activity was not particularly disorganized. In some areas no definite abnormalities were noted. Some random slow activity was present, particularly in the occipital region; none of this was of great amplitude. A fairly well organized electroencephalographic pattern was also noted in the case of Levy and Little [11]; some 6 per second activity was observed in the frontal and central regions, but the alpha rhythm was well defined in the occipital region. When the electroencephalographic examination was repeated one year later, numerous delta waves of high amplitude had appeared. While in Levy and Little's [11] case the onset of grand mal convulsions was noted between the taking of the two records, in our case seizures had occurred prior to the recording of the relatively normal electroencephalogram. One is therefore unable to assert that any specific relation exists between the disorganization of electrical activity in the cortex and convulsions in this disease.

From these observations one is led to the conclusion that marked alterations in the cytoplasm of the ganglion cells with damage to neuro-

10. Dide, M., and van Bogaert, L.: Sur l'Idiotie amaurotique juvénile (type Spielmeyer-Vogt), Rev. neurol. **69**:1-42, 1938.

11. Levy, S., and Little, O. A. G.: Juvenile Familial Amaurotic Idiocy (Vogt-Spielmeyer Disease), Arch. Neurol. & Psychiat. **44**:1274-1289 (Dec.) 1940.

fibrils and loss of Nissl substance of the type noted in this case may not be of as great importance in the production of neurologic deficit and disorganization of the normal electroencephalographic pattern as is frequently supposed. The relatively moderate impairment of the cell nuclei and the almost complete intactness of the myelin sheaths and axons, in spite of the long course of the disease, is further indication of relative functional integrity, despite the striking alterations in cell structure.

The failure of most of the subarachnoid channels to fill in the air encephalogram and the elevated cerebrospinal fluid pressure may be correlated with the large size of the brain and the shallow sulci. This was apparently due to the swelling of the ganglion cells and the proliferation of glia.

SUMMARY

A case of the juvenile type of amaurotic family idiocy is described. An attempt is made to correlate the results of neurologic, psychologic, encephalographic and histologic studies, with particular reference to cortical activity. In spite of severe and widespread cellular alterations, many cortical functions were retained, and the electroencephalographic pattern was not especially impaired.

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SURGICAL HISTORY OF TRIGEMINAL NEURALGIA

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It has been said that Hippocrates, Aretaeus, Galen and others referred to trigeminal neuralgia and that the condition was mentioned as early as 400 B. C. Bretschneider,[1] in his monograph on the external neuralgias, referred to the accounts of these ancient writers; none of them, however, was sufficiently accurate to justify the diagnosis of trigeminal neuralgia. Avicenna (980-1036 A. D.), of the Arabic school of medicine, is often cited as having described trigeminal neuralgia, but Lewy,[2] who was the first to translate correctly Avicenna's work, indicated that he dealt with facial paralysis and facial spasm rather than with a disorder affecting the fifth nerve.

According to Lewy, the first authentic case of tic douloureux was recorded by Bretschneider. He, on the other hand, failed to distinguish this case from numerous others in which the condition undoubtedly did not belong to the trigeminal neuralgias. According to Lewy, Johannes Laurentius Bausch, municipal counselor, physician and philosopher, founder and first president of the Imperial Leopoldinian Academy of Natural Sciences in Schweinfurt, Franconia (Bavaria), suffered for years from trigeminal neuralgia. He finally died in 1665 of complications occasioned by this, at that time, incurable disease. The eulogy written by the secretaries of the academy, Dr. Johannes Michael Fehr and Dr. Elias Schmidt, gives an account of Dr. Bausch's illness and death. The outstanding features of the disease as known today are described in this eulogy, which was published in 1672.

During the following year numerous similar cases were reported. Well known in the literature is the instance described by the author and philosopher John Locke.[3] In one of his almanacs he recounted the story of the Countess of Northumberland, wife of the English ambassador to Paris, and gave a detailed account of the signs and symptoms of her

From the Department of Neurosurgery of the Albany Hospital and Medical College, Union University.

1. Bretschneider, H.: Versuch einer Begründung der Pathologie und Therapie der äusseren Neuralgien, Jena, F. Mauke, 1847.

2. Lewy, F. H.: The First Authentic Case of Major Trigeminal Neuralgia, Ann. M. Hist. **10**:247, 1938.

3. Locke, J.: The Celebrated Locke as Physician, Lancet **2**:367, 1828.

illness. This layman's description is accurate enough to permit the diagnosis of trigeminal neuralgia.

André,[4] in 1756, first spoke of trigeminal neuralgia as "tic douloureux." In 1776 Sir John Fothergill [5] gave the first classic description of this disorder. For a long time after this trigeminal neuralgia was referred to as "Fothergill's disease."

The surgical history of trigeminal neuralgia reveals a centripetal approach to the problem. With the passing of time the tendency has been to substitute central and more radical measures for the relatively ineffective peripheral approaches. This history is divisible into four periods—those of operations on the peripheral nerves, on the ganglion, on the sensory root and on the central connections in the brain stem respectively.

The first period in the operative history is concerned with procedures limited to the peripheral nerves. These include neurotomy, neurectomy, extraction of the nerve and nerve stretching.

Neurotomy, simple cutting of the nerve, was performed by Galen [6] as early as 180 A. D. In spite of the ineffectiveness of this operation, it was still being employed as late as 1840. The branches of both the fifth and the seventh nerve were sectioned in the face. In those days these nerves were not differentiated physiologically, and as a result were considered equally responsible for the pain. In the words of Monro, a surgeon of the latter part of the eighteenth century, "two nerves were given to the face lest by accidental division of one the face should be deprived of nervous power altogether."

It remained for Sir Charles Bell,[7] in 1820, to show the folly of this false belief with his clinical and experimental observations which differentiated the fifth and the seventh nerve. In spite of this work, Bell complained that many surgeons of that period continued to section the seventh nerve for the relief of tic douloureux. However, in time Bell's work became universally accepted, and the relation of the trigeminal nerve to tic douloureux was established.

Neurectomy was recommended by Abernethy [8] in 1793 as a means of preventing recurrences of the neuralgia. Many modifications inevitably followed. Von Klein,[9] in 1822, crushed and cauterized the

4. André, N.: Observations sur les maladies de l'urèthre et sur plusieurs faits convulsifs, Paris, Delaguette, 1756, p. 323.

5. Fothergill, J.: Of a Painful Affection of the Face, Med. Obs. Soc. Phys. **5**:129, 1776.

6. Galen, cited by Horsley, Taylor and Colman.[21]

7. Bell, C.: The Nervous System of the Human Body, Washington, D. C., Duff Green, 1833.

8. Abernethy, J.: Surgical and Pathological Essays, London, J. Evans, 1793.

9. von Klein: Ueber die Möglichkeit der Zerstörung des Gesichtsnerven bei seinem Austritt aus dem Schädel, J. d. Chir. u. Augenh. **3**:46-61, 1822.

central end. Malgaigne [10] split the central portion longitudinally and looped it back. Other workers interposed soft tissues between the divided ends. These refinements, the products of cerebration and frustration, were indeed ingenious, but it appears that the time for successful treatment of tic douloureux had not yet arrived.

Evulsion of the peripheral nerve, merely an extension of neurectomy in which a greater portion of the nerve was removed, represented another unsuccessful attempt at therapy. Thiersch [11] developed this method to its fullest degree, attacking all three branches of the trigeminal nerve and removing the nerve almost in its entirety.

Stretching the nerve was first introduced by von Nussbaum [12] in 1872. Vogt,[13] however, first employed it in 1876 for tic douloureux. Unfortunately, he too was unsuccessful.

The operations on the smaller peripheral branches later gave way to those centering about the three divisions of the nerve. Many methods were devised to reach each division. Warren,[14] in 1828, was the first to section a nerve proximal to its foramen. He used the trephine to reach the inferior maxillary nerve. The names of Lücke,[15] Braun,[16] Lossen,[17] Pancoast,[18] Krönlein,[19] Velpeau,[20] Horsley and associates,[21] Carnochan [22] and many others were associated with this operation.

10. Malgaigne, J. F.: Manuel de médecine opératoire, fondée sur l'anatomie normale et l'anatomie pathologique, ed. 4, Paris, Germer-Baillière, 1843, p. 53.

11. Thiersch, C.: Ueber Extraction von Nerven, mit Vorzeigung von Präparaten, Verhandl. d. deutsch. Gesellsch. f. Chir. **18**:44, 1889; cited by Rose.[24]

12. von Nussbaum, J. N.: Blosslegung und Dehnung der Rückenmarksnerven; eine erfolgreiche Operation, Deutsche Ztschr. f. Chir. **1**:450, 1872.

13. Vogt, P.: Die Nerven-Dehnung als Operation in der chirurgischen Praxis; eine experimentelle und klinische Studie, Leipzig, F. C. W. Vogel, 1877.

14. Warren, J.: Cases of Neuralgia, Boston M. & S. J. **1**:1, 1828.

15. Lücke, A.: Ausschneidung des zweiten Astes des Nervus trigeminus nach temporärer Resection des Jochbogens, Deutsche Ztschr. f. Chir. **4**:322, 1875.

16. Braun, H.: Neurektomien des zweiten Astes des Nervus trigeminus nach osteoplastischer Resektion des Jochbeines, Centralbl. f. Chir. **9**:249, 1882.

17. Lossen, H.: Neurektomie des zweiten Astes des Trigeminus nach osteoplastischer Resektion des Jochbeines, nebst Vorschlag zu einer neuen Schnittführung, Centralbl. f. Chir. **5**:65, 1878.

18. Pancoast, J.: New Operation for the Relief of Persistent Facial Neuralgia, Philadelphia M. Times **2**:285, 1871-1872.

19. Krönlein, R. U.: Ueber eine Methode der Resection des zweiten und dritten Astes des N. trigeminus unmittelbar am Foramen rotundum und ovale, Deutsche Ztschr. f. Chir. **20**:484, 1884.

20. Velpeau, cited by Obalinski, A.: Ueber die temporäre Resection des Unterkiefers behufs Vornahme der Neurectomie des dritten Trigeminusastes, Wien. med. Presse **30**:337-340, 1889.

In this first period the operative approach was based on the anatomic distribution of the trigeminal nerve. The results of many of these operations were both sad and ghastly: sad because the pain invariably recurred, and ghastly because the cosmetic result was rarely considered. The removal of bone and tissue was undertaken with few scruples by the surgeon in an attempt to reach the nerve.

The second period in the operative history is concerned with the gasserian ganglion. Carnochan, in 1858, first proposed removal of this ganglion. For nearly thirty years the operation remained unrecognized, until Abbé,[23] in 1889, employed Carnochan's approach in a case of tic douloureux. Two years later (1891) Horsley and associates [21] devised an operation in which the gasserian ganglion was removed by a temporal approach, but in the 1 case in which it was attempted the patient died. Credit for the first successful removal of the gasserian ganglion and the peripheral nerves belongs to Rose,[24] who in 1892 approached the ganglion by trephining the base of the skull through the pterygoid region. The operative approach which enjoyed the most success was developed by Hartley,[25] also in the same year. He reached the ganglion through the temporal region immediately above the zygoma.

With the increased effectiveness of operative relief of pain, neurosurgeons turned their efforts toward a reduction in the complications and the mortality. Tiffany,[26] in 1896, suggested the refinement of partial ganglionectomy in an effort to reduce the postoperative trophic disturbances of the cornea. He based his proposal on 2 observations which he derived from a review of 108 operations on the ganglion, in which the methods of Rose,[24] Hartley,[25] Krause,[27] Horsley and associates [21] and Doyen [28] were used. Tiffany stated:

> The first division is never involved alone, involvement being due entirely to reflex irritation. . . . Complications ensue when the first branch is removed.

21. Horsley, V.; Taylor, J., and Colman, W. S.: The Various Surgical Procedures Devised for the Relief or Cure of Trigeminal Neuralgia, Brit. M. J. **2**:1139, 1191 and 1249, 1891.

22. Carnochan, J. M.: Exsection of the Trunk of the Second Branch of the Fifth Pair of Nerves, Beyond the Ganglion of Meckel, for Severe Neuralgia of the Face, with Three Cases, Am. J. M. Sc. **35**:134, 1858.

23. Abbé, R.: The Surgical Treatment of Inveterate Tic Douloureux, New York M. J. **50**:121, 1889.

24. Rose, W.: Abstracts of the Lettsomian Lectures on the Surgical Treatment of Trigeminal Neuralgia, Lancet **1**:71, 182 and 295, 1892.

25. Hartley, F.: Intracranial Neurectomy of the Second and Third Divisions of the Fifth Nerve, New York M. J. **55**:317, 1892.

26. Tiffany, L. M.: Intracranial Operations for the Cure of Facial Neuralgia, Ann. Surg. **24**:575, 1896.

27. Krause, F.: Entfernung des Ganglion Gasseri und des central davon gelegenen Trigeminusstammes, Deutsche med. Wchnschr. **19**:341, 1893.

28. Doyen, E.: Extirpation of the Gasserian Ganglion, Ann. Surg. **23**:69, 1896.

Another proposal of Tiffany's was to modify the Hartley-Krause operation so as to preserve the motor root. Cushing,[29] in 1900, developed the "infra-arterial" approach to the ganglion in an effort to reduce further the operative mortality. In this operation the zygoma was resected and the trephine opening made beneath the arch of the middle meningeal artery.

The third period in the operative history was introduced by Frazier and Spiller,[30] but it actually goes back to Horsley's unsuccessful attempt in 1891 to remove the gasserian ganglion, with section of the sensory root. If Horsley's patient had lived the benefits of this operation might have been recognized earlier. The high mortality in ganglionectomies led Frazier and Spiller to seek an operation with less danger to the patient. The results of their experiments developed into the operation in which the sensory root is sectioned—"a physiological extirpation of the Gasserian ganglion." The first successful operation of this type was performed by Frazier in 1901, in which the sensory root was approached by the Hartley-Krause technic. Although the motor root was sectioned at this operation, Frazier maintained that it could be spared.

Spiller and Frazier,[30a] Bregmen [31] and van Gehuchten [32] performed excellent histoanatomic studies of the trigeminal pathways. These investigators observed that a definite anatomic relation exists between the various components of the trigeminal nerve, not only in the peripheral divisions but in the ganglion, the sensory root and the spinal root. They noted that the ventral portion of the spinal root corresponds to the medial portion of the sensory root and the dorsal portion of the spinal root to the lateral portion of the sensory root. Thus, since the central and peripheral prolongations of the gasserian ganglion preserve a definite spatial arrangement, it was reasoned that the ganglion also must have a definite order of arrangement. Tiffany's suggestion of

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29. Cushing, H.: A Method of Total Extirpation of the Gasserian Ganglion for Trigeminal Neuralgia by a Route Through the Temporal Fossa and Beneath the Middle Meningeal Artery, J. A. M. A. **34**:1035 (April 28) 1900.

30. (*a*) Spiller, W. G., and Frazier, C. H.: The Division of the Sensory Root of the Trigeminus for the Relief of Tic Douloureux, Univ. Pennsylvania M. Bull. **14**:341, 1901. Frazier, C. H., and Spiller, W. G.: Physiologic Extirpation of the Ganglion of Gasser: Further Report on Division of the Sensory Root for Tic Douloureux, Based on the Observations of Four Cases, J. A. M. A. **43**:943 (Oct. 1) 1904.

31. Bregmen, E., in Obersteiner, H.: Arbeiten aus dem Institut für Anatomie und Physiologie des Centralnervensystems an der Wiener Universität, Leipzig, F. Deuticke, 1892, pp. 88-92.

32. van Gehuchten, A.: The Surgical Treatment of Trifacial Neuralgia, Univ. Pennsylvania M. Bull. **17**:50, 1904.

sparing the inner third of the ganglion in order to preserve vision was thus substantiated.

It was felt that at last the ideal treatment for tic douloureux had been found. But some of the complications of the operation on the sensory root, such as trophic ulceration of the cornea and paralysis of the motor division of the trigeminal nerve, were still to be eliminated. Frazier,[33] in 1921, offered a refinement in which the motor root was spared. He suggested the use of an electrode not only to identify this root but to allay any fear that a sensory fasciculus was left behind. In 1925 he[34] employed subtotal resection of the sensory root, with section only of the outer two thirds. A still more precise refinement was instituted in 1928 by Stookey,[35] who advocated the differential section of the sensory root, depending on the area of the face involved.

Dandy,[36] in 1925, developed the suboccipital approach to the sensory root at the pons. With this pontile approach he succeeded in avoiding the complications commonly met with in the temporal approach.

The fourth period in the operative history is still in the formative stage. It is concerned with section of the tract in the brain stem. Anatomically, section of the tract is ideal because it eliminates only the pain fibers. Serra and Néri,[37] in 1936, sectioned the quintothalamic tract. Sjöqvist,[38] in 1938, sectioned the bulbospinal tract of the trigeminal nerve within the medulla oblongata. Unfortunately, serious complications from this operation have been reported. Olivecrona[39] has already suggested an improvement in the technic which supposedly eliminates the danger of laryngeal palsy and disturbance of gait and station. However, too short a period has elapsed for the proper evaluation of these procedures.

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33. Frazier, C. H.: A Refinement in the Radical Operation for Trigeminal Neuralgia, J. A. M. A. **76**:107 (Jan. 8) 1921.

34. Frazier, C. H.: Subtotal Resection of Sensory Root for Relief of Major Trigeminal Neuralgia, Arch. Neurol. & Psychiat. **13**:378 (March) 1925.

35. Stookey, B.: Differential Section of Trigeminal Root in Surgical Treatment of Trigeminal Neuralgia, Ann. Surg. **87**:172, 1928.

36. Dandy, W. E.: Section of Sensory Root of Trigeminal Nerve at Pons, Bull. Johns Hopkins Hosp. **36**:105, 1926; An Operation for the Cure of Tic Douloureux, Arch. Surg. **18**:687 (Feb.) 1929.

37. Serra, A., and Néri, V.: Die elektro-chirurgische Unterbrechung der Zentralbahnen des V. Paares am lateralen ventralen Rand des Pons Varoli als erster Behandlungsversuch von hartnäckigen Neuralgien des Trigeminus durch Tumoren der Schädelbasis, Zentralbl. f. Chir. **63**:2248, 1936.

38. Sjöqvist, O.: Eine neue Operationsmethode bei Trigeminusneuralgie. Durchschneidung des Tractus spinalis trigemini, Zentralbl. f. Neurochir. **2**:274, 1938; Trigeminal Neuralgia: A Review of Its Surgical Treatment and Some Aspects of Its Etiology, Acta chir. Scandinav. **82**:201, 1939.

39. Olivecrona, H.: Tractotomy for Relief of Trigeminal Neuralgia, Arch. Neurol. & Psychiat. **47**:544 (April) 1942.

Although tic douloureux today is curable, little if anything is known of its cause. Many theories have been advanced; none so far has proved accurately to explain its cause.

The centripetal development of operative procedures for tic douloureux indicates a distinct advancement in surgical science. In the words of Oliver Wendell Holmes, "The great thing in this world is not so much where we stand, as in what direction we are moving."

Dr. E. H. Campbell and Dr. T. J. C. von Storch gave helpful criticism and suggestions.

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FOREIGN BODY GRANULOMAS PRODUCED BY SURGICAL COTTON

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A case of fatal adhesive or proliferative arachnoiditis resulting from particles of surgical cotton (cottonoid [1]) left at operation prompted the study of which this paper is a report. Because of the observations in this case we have reexamined all of the material we had available in cases in which autopsy had followed operation or in which a previous operation had been done, and in nearly every instance we found that occasional cottonoid fibers had been left and that about them there was a foreign body reaction of a granulomatous type. In most of the specimens the amount of cottonoid was scant and the amount of tissue reaction so slight that it could hardly have been of clinical significance. Yet we feel that in many instances some fibers of cotton or cottonoid left in the wounds, depending on the amount and location, are capable of producing a reaction that will obstruct circulation of the cerebrospinal fluid.

It has been known for many years that cotton buried in tissues produces granulomas (Spies, Mandeville and Awdziewicz [2]). Nevertheless, though pledgets of cotton or the proprietary preparation cottonoid have been widely used as absorbent sponge material during neurosurgical operations, we have found no reference to this subject. The lack of previous clinical reports may be explained by the fact that since the cellulose fibers are relatively inert chemically, they do not stain by any of the ordinary methods and are, therefore, not readily visualized by

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From the Departments of Neurosurgery and Pathology, Good Samaritan Hospital.

1. Cottonoid is described by Johnson & Johnson as "a compressed lightly-embossed and lightly-sized cotton sheet. It is prepared from a web of our best grade surgical cotton (i. e., comparable to Red Cross cotton), which stock is passed under an embossing roll with a light sizing solution, the pressure and size contributing toward bonding and strengthening of the sheet. This size bath consists of approximately 2% dextrinized corn starch and 0.8% boric acid."

2. Spies, J. W.; Mandeville, F. D., and Awdziewicz, F. J.: Nature and Result of Animal Tissue Reactions to Cellulose, Proc. Soc. Exper. Biol. & Med. **30**:420-425, 1933.

the transmitted light of the standard microscope. When sections containing cottonoid are studied under polarized light, the fibers of cellulose stand out brightly in the darkened field.

The case of adhesive arachnoiditis referred to in the opening paragraph justifies a brief report.

REPORT OF A CASE

Sister M. D., a white woman aged 23, was admitted to the Good Samaritan Hospital in Cincinnati on Nov. 15, 1939 with the complaint of recurring bouts of vertigo and slight tinnitus in the left ear. She had not experienced headache. The fundi were normal. There was hypesthesia of the left cornea. During the bouts of vertigo, nystagmus was present, and there was pronounced unsteadiness of gait, with a tendency to fall to the left. Between the bouts there was no ataxia and no alteration of gait and station.

On November 18 a lumbar puncture was done. The initial pressure, with the patient in the horizontal position, was 140 mm. of water. The fluid was clear and colorless. The cell count was 0; the protein content was 30 mg. per hundred cubic centimeters, and the Wassermann reaction was negative.

Roentgen examination of the skull revealed no pathologic change.

Prior to admission, intensive medical therapy (potassium chloride and histamine phosphate) had been given for several months, without benefit. It was suspected that the patient had a tumor in the left cerebellopontile angle, and it was decided to explore this area, with the plan of dividing the vestibular portion of the eighth nerve if no tumor was encountered.

On November 27, with the use of procaine anesthesia, the left cerebellar fossa was explored. No tumor was seen. The vestibular portion of the eighth nerve was divided. During the course of the operation a pledget of cottonoid, identified with a silk suture, was placed between the tonsils of the cerebellum to prevent oozing blood from entering the fourth ventricle. On the fourth postoperative day, the patient had begun to complain of severe headache and showed evidence of increased intracranial pressure. A lumbar puncture released blood-tinged fluid under 350 mm. of pressure.

Because a hematoma was suspected, the wound was reopened on Dec. 1, 1939. There was about 1 teaspoon of clotted blood in the extradural space. The tonsils of the cerebellum were adherent to each other. They were released. Immediately after operation the patient appeared in good condition, but three days later there was again evidence of increased intracranial pressure. Attempts to control this pressure by repeated ventricular and spinal taps were unsuccessful.

On Jan. 5, 1940 ventriculographic examination and exploration of the posterior fossa were carried out. The arachnoid and pia about the lower pole of the cerebellum were greatly thickened, and the cerebellar tonsils were densely adherent to each other, so that the foramen of Magendie was occluded. Insofar as possible, the normal pathways of the cerebrospinal fluid were reestablished by separation of the adherent surfaces, and for about ten days the intracranial pressure seemed to be controlled. Thereafter, the area of decompression again began to bulge, and it was obvious that the circulation of the cerebrospinal fluid was again obstructed.

On January 19 a third ventriculostomy was done; except for moderate hyperthermia, the patient did fairly well until the end of the third day, when she had a sudden convulsive seizure. Thereafter, she remained in coma until her death, six hours later.

Autopsy was performed three hours after death. There was nothing remarkable about the cerebral hemispheres, except for marked dilatation of the entire ventricular system and the surgical opening in the wall of the third ventricle. About the brain stem, however, the leptomeninges were greatly thickened, and this reaction spread over the inferior surface of the cerebellum. The cerebellar tonsils were densely adherent to each other, and the foramen of Magendie was occluded. In the upper portion of the fourth ventricle there was a small tumor nodule, measuring 7 mm. in diameter. This tumor, on microscopic examination, proved to be an ependymoma of low grade malignancy. We were convinced that it was not of sufficient size to have occluded the fourth ventricle.

Microscopic examination of the thickened leptomeninges showed an extensive productive reaction characterized by the formation of granulomas, which in certain areas bore a striking resemblance to tubercles. Associated with the granulomas were diffuse proliferation of fibroblasts, much edema and a collection of lymphocytes and giant cells. Under polarized light, there were seen numerous fragments of cottonoid material, each fragment serving as a nucleus for the formation of a granuloma. There was no evidence of pyogenic infection (fig. 1).

OTHER MATERIAL

In all, 12 specimens from operative cases were reexamined. In 8 of the 12 cases we were able to find an occasional fiber of cottonoid, and in each instance a granuloma surrounded the fiber.

In figure 2 are shown sections of a granuloma observed at autopsy in the bed from which an acoustic neurinoma had been removed. The patient had bilateral acoustic neurinoma and a meningioma in the posterior fossa. Death followed the attempt to remove an acoustic neurinoma on the right side.

COMMENT

This group of cases had one thing in common, the production of foreign body granulomas. These granulomas were characterized by a tissue reaction consisting of the proliferation of fibroblasts, with some of the cells resembling epithelioid cells; the accumulation of certain wandering cells, most of which were monocytes and lymphocytes, and the appearance of multinucleated giant cells about foreign body elements, which in this instance were cellulose fibers. In certain cases the granulomas resembled tubercles, and in 1 instance the resemblance was so striking that special stains were carried out to eliminate the presence of tuberculosis.

For the most part, the granulomas occur, as might be supposed, in the arachnoid and cause extensive chronic productive arachnoiditis, which, depending on the degree and location, may lead to obstructive phenomena. When the cellulose material is scanty, its recognition may be difficult. Of great aid in its identification is the use of polarized light.

It was interesting to note in the specimens examined that when the field of operation was small, so that pledgets of cottonoid were repeatedly

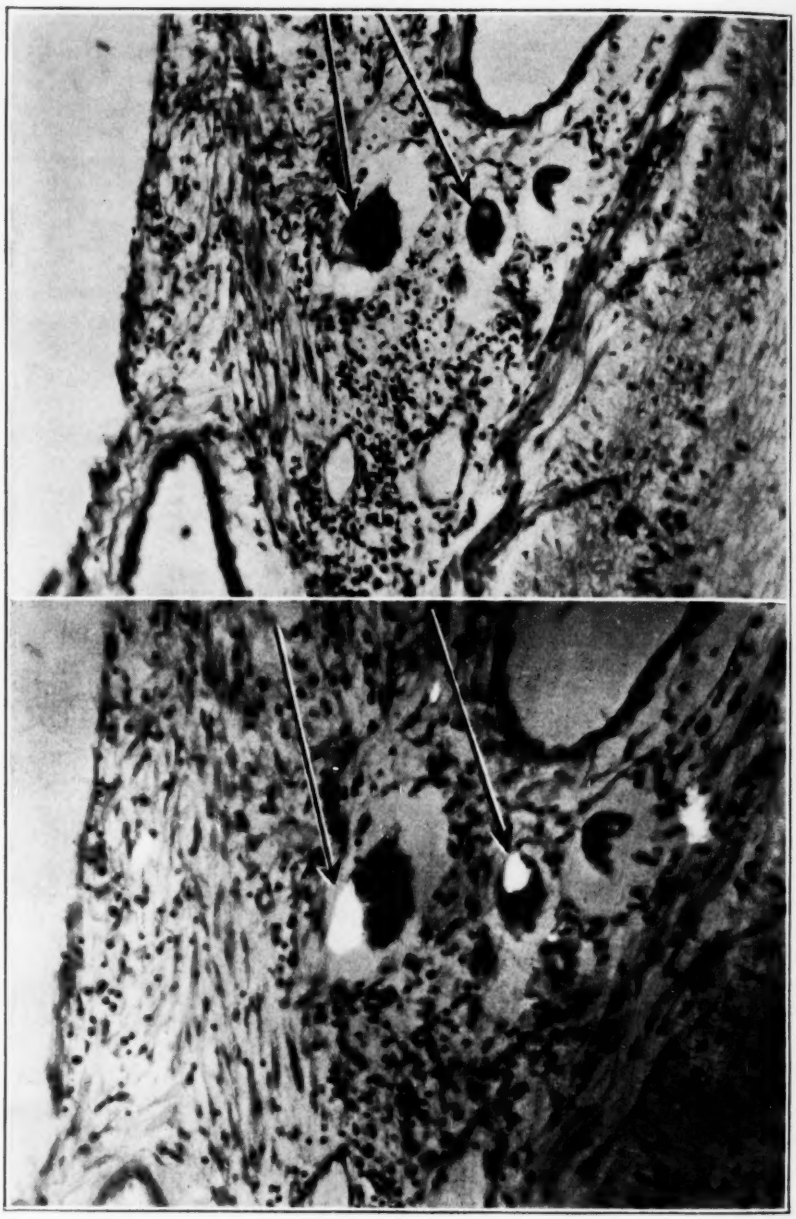

Fig. 1.—Tuberculous-like reaction in the human basilar meninges produced by cottonoid used as a surgical sponge. With ordinary illumination (above) the cottonoid fibers which are being attacked by giant cells in the arachnoid, escape attention, while with polarized light (below) the material becomes obvious.

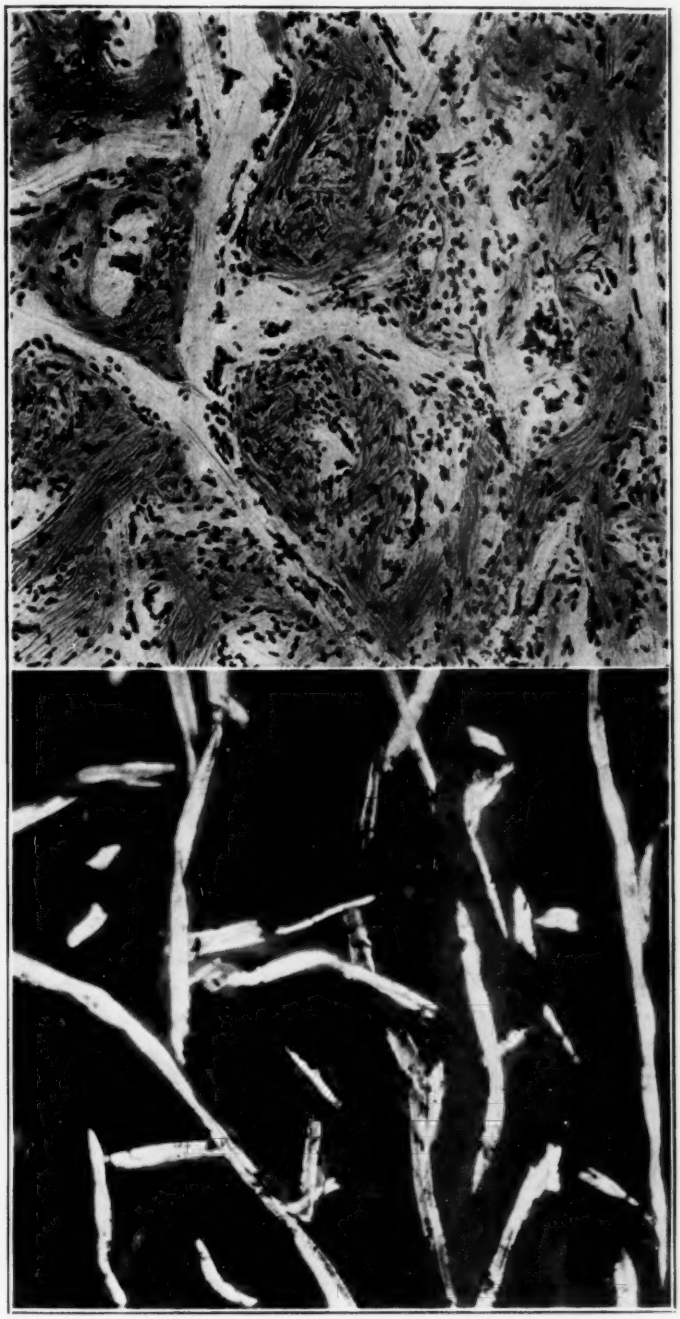

Fig. 2.—Above, photomicrograph of a thickened arachnoid viewed with ordinary illumination and slightly out of focus. The cottonoid fibrils are barely perceptible. Below, the same microscopic field viewed with polarized light. The same fibrils stand out dramatically in illumination against a darkened field. Hortega silver impregnation.

pushed in and out of small openings, the amount of material left was greater. When the field of exposure was large, the amount left was minimal.

It is not our intention to condemn the use of cotton or cottonoid. However, it does seem well, in view of the general use of these materials, to call attention to the possibility of fibers being detached and left in the field of operation. Thorough irrigation of the wound would probably remove all particles. Cottonoid has been used exclusively by us as absorbent sponge material in preference to standard cotton. We do not feel that the reaction described is the result of any inherent chemical property of this proprietary product, but rather that it would occur as a response to any nonabsorbable foreign body left in the tissues.

SUMMARY

A case of fatal adhesive arachnoiditis resulting from foreign body reaction to surgical cotton is reported. Observations in other cases in which fibers of this material were left at operation are commented on.

COMPARISON OF METRAZOL CONVULSIVE THERAPY WITH ELECTRIC SHOCK IN TREATMENT OF SCHIZOPHRENIA

EVALUATION OF RESULTS OBTAINED IN TREATMENT OF ONE HUNDRED SCHIZOPHRENIC PATIENTS WITH ELECTRIC SHOCK

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In 1940 I reported[1] results obtained in the treatment of 100 schizophrenic patients with metrazol convulsive therapy. A similar study has been conducted during the past one and one-half years in the treatment of 100 schizophrenic patients with electric shock. The present group was composed approximately of the same type of psychiatric material as that employed in the first study.

It has been emphasized by several writers that the difference in diagnostic criteria used by various clinicians in arriving at the diagnosis of schizophrenia is responsible for contradictory reports as to the results obtained with shock therapy in many hospitals. It is even debatable at present whether the term schizophrenia is actually limited to one mental disorder or may include a variety of similar psychiatric conditions. Besides, patients seen by psychiatrists in private practice and outpatient mental hygiene clinics are often of different type than those committed to public institutions. In psychiatric clinics one is apt to see more patients with borderline disorders without deterioration. In private hospitals patients are encountered of higher social, economic and educational level. Hence, tremendous discrepancies are noticed in the reports on results obtained with shock therapy by various workers in all sorts of institutions.

MATERIAL

The present study was made on patients admitted to the same public hospital, which derives patients from a comparatively small community of approximately the same social level as that represented two years ago when the results with metrazol-treated patients were reported. The two groups were essentially the same, and special effort was made to compare each group as to type of schizo-

1. Reznikoff, L.: Evaluation of Metrazol Shock in Treatment of Schizophrenia: Report of Results in One Hundred Cases, Arch. Neurol. & Psychiat. **43**:318-325 (Feb.) 1940.

phrenia, duration of psychosis, mode of onset and precipitating factors, duration of hospitalization prior to treatment, age, sex, factors of chronicity, tendency to deterioration and hospital atmosphere, including psychologic influences during the administration of shock therapy.

Each group included only patients whose condition could be diagnosed as schizophrenia without the slightest doubt. All patients in each group were presented at the staff conference before administration of shock therapy, so that only patients whose psychosis was definitely diagnosed as schizophrenia were used in this study. At the completion of treatment, they were again presented at the staff conference and classified as "with remission," "much improved," "improved" and "not improved" (these terms having been in a previous communication [1]).

PROCEDURE

Since the technic of administration of electric shock therapy has been adequately described in many papers and is comparatively simple, it seems unnecessary to repeat it here. The electric shock machine manufactured by Rham, Inc., was used in this work. Treatment was given three times a week.

Of the 100 patients, 42 were men and 58 women. A total of 1,921 treatments was given, of which 1,160 resulted in generalized convulsive seizures. All degrees of reactions could be observed during the application of electric shock. At times, with a low voltage for a given patient, only slight flushing of the face or pallor and blinking of the eyelids were obtained. At other times typical petit mal attacks or intermediate reactions between petit and grand mal, or even abortive attacks of grand mal might result. However, it seems that generalized convulsive seizures that look like attacks of grand mal epilepsy must be produced in order to achieve therapeutic effect. A few patients treated with only petit mal attacks, because of mild contraindications, improved only slightly, and a drastic difference was noted when the type of convulsions induced was changed from petit to grand mal. In some exceptional cases, in which extreme caution was required because of an obvious physical contraindication, a course of petit mal attacks might be attempted. Ordinarily, if a grand mal seizure was not produced, another treatment was given in five to ten minutes; no harm was observed when this interval was shortened to two minutes. In fact, in 2 or 3 shock-resistive patients, when a grand mal seizure could not be induced with the highest voltage available with this machine, another treatment was given at once, with production of the desired generalized convulsion. Several other measures may be taken to produce a generalized seizure in patients who require higher voltage. For example, the interval between treatments may be lengthened from three times to twice a week, and in some exceptional cases even to once a week. An attempt was made to reduce the convulsive threshold by alkalinizing the patients with large doses of sodium bicarbonate. This procedure, however, was unsuccessful. In general, it may be stated that one rarely encounters this difficulty, that it does seem to occur more often in women than in men (perhaps because of thicker growth of hair over the area where the electrodes are applied) and that it is present in some older patients.

Since only schizophrenic patients were included in this group, the oldest was 53 and the youngest 15 years of age. As with metrazol treatment, the majority of patients gained weight, and only a few lost. However, the gain in weight with electric shock was considerably lower than that with metrazol. The average gain in weight with electric shock amounted to 6.4 pounds (2.9 Kg.) and that with

metrazol to 9.14 pounds (4.2 Kg.). It has also been noticed that the patients who failed to gain weight reacted poorly to the treatment and did not improve. Patients were allowed to have 8 to 12 generalized convulsive seizures; a few had 15; the average was 11.6 generalized convulsive attacks. A few patients relapsed two or three weeks after therapy was completed and then were given a few additional treatments, while 9 patients received a complete additional course after six to twelve weeks. In the metrazol-treated group, at first as many as 40 convulsive seizures of grand mal type were produced, and only later was it considered that if there was no improvement with 20 or 25 grand mal seizures further administration of metrazol therapy was useless, since in some patients satisfactory results were obtained with 10 seizures. Because the electric shock era followed the use of metrazol, some knowledge had been gained from electroencephalographic studies which indicated that rather persistent abnormal waves may follow prolonged convulsive therapy.[2] It seems best now not to allow a patient to have more than 12, or at the most 15, generalized convulsive attacks in one course of treatment. This caution is especially warranted since up to the present sufficiently comprehensive microscopic studies of human brain tissue after electric shock have not been made, obviously owing to lack of material.[3]

The longest duration of psychosis among the patients in this group was about ten years and the shortest six weeks. The average duration of illness was twenty-four and four-tenths months. According to the duration of psychosis, the patients were divided into four groups:

Duration	No. of Patients
Under 6 months	29
6 months to 2 years	40
2 years to 5 years	18
Over 5 years	13

They were classified as to the type of schizophrenia as follows:

Type	No. of Patients
Catatonic	20
Paranoid	63
Hebephrenic	14
Simple	3

RESULTS

Since relapses following any kind of shock therapy for schizophrenia are rather frequent, it is important to keep in mind that statistical results obtained immediately after treatment will differ considerably from those compiled after several months of observation of the patient.

In this group of patients, if remission was not maintained and the patient relapsed in a few weeks, he was classified as unimproved. The

2. Davis, P. A., and Sulzbach, W.: Changes in the Electroencephalogram During Metrazol Therapy, Arch. Neurol. & Psychiat. **43**:341-353 (Feb.) 1940. Pacella, B. L., and Barrera, S. E.: Some Considerations of the Electroencephalogram in the "Convulsive State," J. Nerv. & Ment. Dis. **96**:125-129 (Aug.) 1942.

3. Alpers, B. J., and Hughes, J.: Changes in the Brain After Electrically Induced Convulsions in Cats, Arch. Neurol. & Psychiat. **47**:385-398 (March) 1942.

present report was prepared two to eighteen months after completion of the treatment; that is, the first patient completed treatment with electric shock eighteen months ago and the last patient only two months ago. Table 1 shows the results of treatment according to the duration of schizophrenia, including the relapses.

As is seen in table 1, 68 patients were unimproved and 32 patients were improved (of these, 13 patients were classified as having achieved remission, 4 patients were much improved and 15 patients were improved). In the metrazol-treated group after relapses were taken into consideration, approximately the same results were obtained. In both groups better results were obtained in patients with a shorter duration of mental illness. Of the 29 patients treated with electric shock who were ill less than six months, 14 improved and 15 failed to improve, while in the group of 31 patients with duration of psychosis of more

TABLE 1.—*Results of Treatment According to Duration of Schizophrenia, Including Relapses*

Duration of Psychosis	No. of Patients	Patients with Remissions		Patients Much Improved		Patients Improved		Patients Not Improved	
		No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Under 6 mo.	29	8	27.6	1	3.5	5	17.2	15	51.7
From 6 mo. to 2 yr.	40	4	10.0	2	5.0	8	20.0	26	65.0
From 2 to 5 yr.	18	0	0.0	1	5.55	1	5.55	16	88.9
Over 5 yr.	13	1	7.7	0	0.0	1	7.7	11	84.6
Total	100	13		4		15		68	

than two years only 4 improved. It is difficult to say why some schizophrenic patients, even with a psychosis of relatively short duration, do not show any improvement, or very slight symptomatic change, while others achieve apparent remission, even though temporary. As with the metrazol method, one is frequently impressed with the rather sudden change in behavior of mute, negativistic, catatonic patients. But while they become better institutional patients and are easier to manage and their pronounced catatonia disappears, they frequently remain apathetic or relapse after a short time into an indifferent, emotionally shallow state and otherwise show the familiar schizophrenic pattern.

Table 2 gives detailed information as to the results obtained with each type of schizophrenia. It is interesting to note that of 20 catatonic patients, 9 improved and 11 failed to improve. Of 3 patients suffering from a simple type of schizophrenia, none improved. Only 2 schizophrenic patients who had been ill longer than five years improved, but when their case histories are studied, one finds that they had had several spontaneous remissions in the past and did not require continuous institutionalization. The impression is gained that convulsive shock

therapy shortens the duration of hospitalization and brings about improvement in patients who are inherently capable of spontaneous improvement.

COMPLICATIONS

The same contraindications and precautions considered for metrazol-induced convulsions are applicable in the use of electric shock. All patients prior to treatment had careful physical and neurologic examinations, and a roentgenogram of the chest, an electrocardiogram and serologic tests were made. On completion of treatment, they were submitted to another electrocardiographic test. The blood pressure was taken before treatment, immediately after the seizure and thirty minutes after treatment was given. At the end of the convulsive attack there were observed a considerable rise in the systolic blood pressure and a

TABLE 2.—*Results of Treatment According to the Type and the Duration of Schizophrenia, Including Relapses*

	Catatonic				Paranoid				Hebephrenic				Simple			
	Under 6 Mo.	6 Mo. to 2 Yr.	2 Yr. to 5 Yr.	Over 5 Yr.	Under 6 Mo.	6 Mo. to 2 Yr.	2 Yr. to 5 Yr.	Over 5 Yr.	Under 6 Mo.	6 Mo. to 2 Yr.	2 Yr. to 5 Yr.	Over 5 Yr.	Under 6 Mo.	6 Mo. to 2 Yr.	2 Yr. to 5 Yr.	Over 5 Yr.
Patients with remissions	4	1	0	0	3	3	0	1	1	0	0	0	0	0	0	0
Patients much improved	0	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0
Patients improved	0	1	0	0	2	6	1	0	3	1	0	1	0	0	0	0
Patients not improved	4	7	0	2	10	16	11	7	1	2	3	2	0	2	1	0

drop in the diastolic pressure, but in a half-hour the blood pressure returned to the original level. During the treatment a small sandbag was placed between the shoulders, and the extremities were held downward. A tongue depressor well padded with gauze was kept between the teeth during the treatment. There were several dislocations of the lower jaw, which, however, did not present any difficulty; at the end of the convulsive seizure the jaw either dropped in place by itself, or the dislocation was easily reduced by the physician. One male patient had a fracture of the right hip, and another suffered an impacted fracture of the neck of the left humerus. Electrically induced convulsions seem milder than metrazol convulsions and, according to the claims of some workers,[4] are less apt to cause fractures. There were no deaths in this series.

4. Smith, L. H.; Hughes, J.; Hastings, D. W., and Alpers, B. J.: Electroshock Treatment in the Psychoses, Am. J. Psychiat. **98**:558-561 (Jan.) 1942. Worthing, H. J., and Kalinowsky, L. B.: The Question of Vertebral Fractures in Convulsive Therapy and in Epilepsy, ibid. **98**:533-537 (Jan.) 1942.

Prolonged apnea occurred more often with electric shock than with metrazol; at times it was alarming, but in all my patients consciousness returned without application of artificial respiration. Cyanosis appeared deeper with electric shock than with metrazol therapy.

Vomiting was met with in an occasional patient, usually only after the first or second treatment, and was much rarer than with metrazol.

Psychomotor hyperactivity following treatment occurred only in exceptional cases and was much milder and lasted a shorter time than after metrazol. The restlessness, extreme fright and at times regression observed during metrazol treatment, especially after incomplete reactions, were practically eliminated with electric shock.

Amnesia for treatment and relative lack of anxiety and fear are perhaps the greatest advantages of electric shock over metrazol therapy. At times, however, in some patients apprehension was noticed, which was more marked for the first few treatments and gradually disappeared as the patient learned not to fear the treatment. A few patients, however, remained fearful throughout the treatment, although the fear was not as extreme as was commonly observed with metrazol.

The onset of the convulsive seizure was almost instantaneous after application of the electric shock, although in some patients the latent period was observed to last from a few seconds to ninety seconds, but this was rare. It was definitely shorter than with metrazol. Latent convulsive attacks were not observed with electric shock.

Neubuerger, Whitehead, Rutledge and Ebaugh,[5] in a study of pathologic changes in the brains of dogs given repeated electric shocks, stated:

> Some degree of neuropathologic change is to be expected in animals given electric shock of the same strength and duration as those observed clinically. Our results suggest that the histologic changes induced by electric shock in the brains of dogs are somewhat less severe than the changes we found following metrazol.

SUMMARY AND CONCLUSIONS

Approximately the same results were obtained in 100 schizophrenic patients treated with electric shock as in a similar group of patients treated with metrazol. Two to eighteen months after treatment was completed, 32 patients were improved and 68 were unimproved.

There is a pronounced tendency to relapse in schizophrenic patients treated with convulsive shock therapy.

While amelioration of psychotic symptoms and behavior occurs in many patients, the essential schizophrenic pattern remains unchanged.

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5. Neubuerger, K. T.; Whitehead, R. W.; Rutledge, E. K., and Ebaugh, F. G.: Pathologic Changes in the Brains of Dogs Given Repeated Electrical Shocks, Am. J. M. Sc. **204**:381-387 (Sept.) 1942.

Convulsive shock therapy helps to achieve remissions earlier than routine institutional treatment and therefore diminishes the duration of hospitalization.

Electric shock therapy is preferable to metrazol therapy, as has been pointed out by many workers, because there are amnesia for the treatment, less fear and anxiety, painless shock and avoidance of repeated intravenous injections in resistive patients.

Its greatest value consists in aiding in the preparation of uncooperative patients for other therapeutic measures, such as psychotherapy, occupational and recreational therapy and general psychiatric management.

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NEUROPSYCHIATRIC SEQUELAE OF PARTIAL EXSANGUINATION

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Experimental observations on animals in which complete or temporary arrest of the cerebral circulation has been effected indicate that profound clinical and pathologic sequelae are consequent on the procedure. Gildea and Cobb [1] discovered that periods of total anemia of no longer than ten minutes resulted in severe, permanent lesions of a necrobiotic character in the cerebral cortex of the cat. Using the dog as subject, Kabat and Dennis [2] produced unconsciousness, cessation of respiration and total abolition of reflexes by obstruction of the cephalic blood flow for fifteen to twenty minutes. The chronic picture was one of virtual decerebration.

The exact human counterpart of these controlled investigations is necessarily difficult to find. Several cases have been reported, however, in which sudden, and presumably complete, cerebral anemia was followed by the development of neuropsychiatric syndromes. Postmortem examination revealed the expected irreparable and extensive damage to the brain. The factors productive of ischemia in these cases were loss of blood and fall of intravascular pressure, singly or together. Wolf and Siris,[3] under the heading "acute non-traumatic encephalomalacia," described the rapid advent of unconsciousness and the protean signs of neurologic deficit in 4 elderly patients who were operated on for neurosurgical conditions in the upright position. A precipitous and extreme drop in blood pressure occurred during the course of the procedure. Necropsy disclosed bilateral, hemorrhagic infarction involving the cortex and superficial subcortex of the brain, particularly in the parietal regions. None of the cerebral arteries was occluded. The case of another patient in whom evidences of widespread injury to the central nervous system appeared shortly after severe and protracted shock supervened during

From Saint Elizabeths Hospital.

1. Gildea, E. F., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

2. Kabat, H., and Dennis, C.: Decerebration in the Dog by Complete Temporary Anemia of the Brain, Proc. Soc. Exper. Biol. & Med. **38**:864, 1938.

3. Wolf, A., and Siris, J.: Acute Non-Traumatic Encephalomalacia Complicating Neurosurgical Operations in the Sitting Position, Bull. Neurol. Inst. New York **6**:42, 1937.

operation was reported by Schnedorf, Lorhan and Orr.[4] Exploratory laparotomy was conducted with the patient under spinal anesthesia. Coma, convulsive seizures, signs of disease of the pyramidal tract and irrational activity featured the postoperative course, and death occurred on the twenty-first day. The cortical gray matter was observed to be the seat of alterations in the ganglion cells and of devastation necrosis. Symmetric cerebral softening was observed by Foix, Chavany and Bascourret [5] after ictus caused by massive venesection in elderly, arteriosclerotic persons.

These clinical contributions all treat of the relatively acute, fatal consequences of rapidly developing cerebral anemia. An unusual opportunity to study the long term effects of such a disaster was afforded by the case which follows. A middle-aged man, in previous good health, attempted suicide while in an involutional depression. Exsanguination almost resulted in death. Appropriate emergency measures saved his life, but he was left with severe neuropsychiatric disability, which is the subject of consideration.

REPORT OF A CASE

W. L., a 42 year old married white man, a lieutenant in the United States Naval Reserve, was admitted to Saint Elizabeths Hospital on April 14, 1942.

The family history was negative for neuropathic determinants. A short, mild depression followed the death of the patient's first wife. He subsequently remarried, and happily so. He is said to have been in excellent health all of his life.

In January 1942, he was assigned to a ship undergoing commission. Nothing save a tendency to overconscientiousness was remarkable about his conduct. On February 17 he was found unconscious, virtually pulseless and gasping for breath, bleeding from a deep incision in the left side of the neck which transected the external jugular vein and from a similar wound in the left wrist. These lacerations had been self inflicted with a razor blade.

By the time he was discovered the systolic blood pressure was low and the diastolic pressure could not be obtained. He was rushed to a hospital where the incisions were sutured and intravenous transfusions of blood and fluids given. On the third hospital day he was conscious and moderately cooperative but was completely aphasic, confused and disoriented. He was unable to find his way about the ward, dressed and undressed at inappropriate times and made irrelevant remarks.

He was transferred to the United States Naval Hospital, Jacksonville, Fla., on March 6. On admission to that institution neurologic examination revealed pallor of the optic disks, hoarseness of speech, possible diplopia and weakness of the left hand grip. He could not carry out complex commands. Nearly complete motor aphasia existed, and writing was scrawled and repetitious. He was disoriented and affectively obtunded. The total protein content of the spinal fluid was increased,

4. Schnedorf, J. G.; Lorhan, P. H., and Orr, T. G.: The Problem of Anoxia in Surgery and Anesthesia, Arch. Surg. **43**:169 (Aug.) 1941.

5. Foix, C.; Chavany, J. A., and Bascourret: Foyers de ramollissement simultanés dans les deux hémisphères, Rev. neurol. **32**:77, 1925.

and there was a midzonal colloidal gold curve, but the Kahn reactions of the fluid and the blood were negative. He refused to eat at first but later became ravenous. He remained confused and unaware of time or place, but the mood changed to one of quiet cheerfulness. He was removed to the United States Naval Hospital, Washington, D. C., and from there to Saint Elizabeths Hospital.

At the time of entrance to the last hospital the patient was rather happy, friendly and moderately cooperative but appeared dazed. There was no abnormality of mental content. Perception and comprehension were faulty. He was totally disoriented for time and stated that he was in "Tampa—no, no—Washington!" Memory for remote and recent events was impaired, as were retention and recall. He admitted the suicidal attempt, declared that he had been deeply depressed at the time and insisted that such a thing would never happen again.

Formal examination of the receptive, gnostic and expressive capabilities was rendered difficult by the patient's mental confusion and defects in memory. A prominent semantic component was evident in imperfect understanding and responses. The latter were fluctuating in their correctness. Speech was occasionally paraphasic and jumbled. At times he was unable to name common objects correctly, misidentified words on a printed list and could not select articles of the same color. When the examiner whistled such familiar tunes as "Yankee Doodle," he carried on, but could not say which air he was humming. When he was asked to touch his nose with his right hand, he placed his left hand on the top of his head, recognized the failure and said, "I know what I want to do, but I can't do it." He could mimic movements only in a mirror fashion. Complicated commands, involving a temporal component, were consistently misunderstood and misapplied. He read accurately but without comprehension. He wrote his name correctly but put down his home address instead of the requested date. In letters he was forced to fall back on terms of endearment to fill in gaps in thought transmission.

He was unable to perform simple arithmetical calculation. Writing, as noted, often consisted of ejaculations or expletives and was irrelevant. There was decomposition of words. He confused right and left more often than he recognized them, and he misidentified fingers fairly consistently.

Examination of the cranial nerves revealed pallor of the optic disks, weakness of the left lateral rectus muscle with diplopia and hoarseness. The last condition was said to have existed only since the suicidal attempt. Greater power in the left arm than in the right was probably due to the patient's predominant left handedness. The fourth and fifth fingers of the left hand were weak and held in partial flexion. Pinprick was poorly appreciated in the corresponding sensory distribution of the ulnar nerve. He could not perform skilled movements with the left hand. The deep reflexes were accentuated in the legs and in the right arm. The cutaneous reflexes were intact, and there were no abnormal reflex signs.

There was almost complete atopognosia in the hands and feet. Astereognosis and decrease in position sense were present in the left hand. Vibratory sensation was diminished in the left leg to the iliac crest.

The lacerations were well healed. There was no evidence of generalized arteriosclerosis, and the blood pressure was 132 systolic and 80 diastolic. The results of a complete blood count, urinalysis and the Kahn test of the blood were all within normal limits. Indirect inspection of the larynx revealed paresis of the left vocal cord.

A psychometric study was attempted, the report of which follows: "He is so confused that he cannot understand the questions . . . It is useless to evaluate the mental level. He appears to have suffered great cerebral damage" (Dr. Winifred Richmond). The report of the Rorschach test (Dr. Isabelle Kendig) was as

follows: "Severe, organic disease of the brain is indicated. . . . Little can be said of the patient's original makeup, although certain signs which point to an anxious, cautious, meticulous approach to life lend support to the diagnosis of involutional melancholia made at the Navy Hospital."

Repeated electroencephalograms were reported as being "within the range of normal variation" (Dr. Robert Cohn). Occasional waves of long duration were observed in the monopolar derivations.

At the time of this report the condition of the patient was essentially unchanged. He appeared to have recovered from the depression completely.

COMMENT

Briefly summarized, the psychiatric picture was one of severe cerebral degeneration. Intellectual deterioration precluded a more accurate analysis of the coexisting aphasia than the description of it as a mixed receptive-expressive defect, probably of a "transcortical"[6] character. Apraxia was apparently ideomotor in type.

The presence of atopognosia and astereognosis and loss of position and vibratory sensations were striking. These abnormalities, plus the inability of the patient to calculate or write normally, his confusion of right and left and his misidentification of fingers, were indicative of large lesions in the parietal lobes. The last-named signs have been grouped together by Gerstmann[7] as a syndrome, and are usually associated with involvement of the angular gyrus and the middle occipital convolution.

Pallor of the optic nerve heads may have been the result of ischemia. The weakness of the lateral rectus muscle is explicable perhaps on the basis of nuclear injury or compression of the abducens nerve during the time when the intracranial process was most acute. Partial severance of the left recurrent laryngeal nerve or tamponade by extravasated blood probably produced the defect in vocalization. The "ulnar palsy" was undoubtedly the result of the incision of the wrist.

It would seem that a combination of massive loss of blood and rapid fall in blood pressure could best account for the lesions underlying the neuropsychiatric syndrome. Air embolism may have been implicated, but the general extent of the clinical signs and the absence of convulsive seizures tend to eliminate this from consideration as an etiologic agent. The exact nature of the implied pathologic alterations is conjectural. The lesions present were thought to be of two types. The intellectual debilitation, confusion, disorientation and failure of memory could be correlated reasonably with the kind of diffuse necrobiotic changes in the cortex produced by Gildea and Cobb[1] in the experimental animal and

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6. Nielsen, J. M., and FitzGibbon, J. P.: Agnosia, Apraxia, Aphasia, Los Angeles, The Los Angeles Neurological Society, 1936.

7. Gerstmann, J.: Syndrome of Finger Angnosia, Disorientation for Right and Left, Agraphia and Acalculia, Arch. Neurol. & Psychiat. **44**:398 (Aug.) 1940.

observed at autopsy in the case of Schnedorf and associates.[4] The neurologic abnormalities, the "transcortical" character of the aphasia and the existence of the Gerstmann syndrome indicate a more extensive injury in the parietal lobes of the brain. The encephalomalacia observed by Wolf and Siris,[3] as well as Foix and associates,[5] in whose patients injurious factors were similar, was predominantly parietal.

A word might be added concerning the rapid change in the patient's mood following his endeavor to end his life. Whether it was the attempt at suicide per se, sudden physiologic changes in the central nervous system induced by blood letting or subsequent lesions in the frontal areas, a sort of self-administered "shock therapy," or "lobotomy," appears to have been instrumental in the lifting of depression.

SUMMARY

A case of a suicidal attempt during involutional melancholia is reported. Severance of an external jugular vein almost resulted in complete exsanguination and death. Examination of the patient two months after the injury revealed evidences of extreme intellectual deterioration. The mood had changed to one of cheerfulness. A mixed receptive-expressive aphasia with a large semantic component and "transcortical" features existed. The patient was also apraxic. The principal neurologic signs were those associated with disease of the parietal lobes, and the Gerstmann syndrome was present. Diffuse cortical lesions of a focal ischemic character and larger infarcts induced by sudden cerebral anemia were thought to represent the pathologic substrate of the clinical picture. The possible relationship of the episode to the cessation of mental depression is commented on.

Saint Elizabeths Hospital.

News and Comment

COURSE OF STUDY IN THE RORSCHACH TEST IN DIAGNOSIS OF THE MILDER MENTAL DISORDERS

The Michael Reese Hospital announces that Dr. S. J. Beck (Ph.D.) will offer his usual course this year on the Rorschach test. Accent will be on the less serious mental disturbances in which success in treatment appears possible. The differentiating patterns of responses to the test, for patients with such disorders, will be studied from full response records and will be contrasted with those obtained from patients with more serious conditions.

The course will be in session 2 two hour periods daily for five days, June 7 to 11, 1943, inclusive. Interested persons are invited to communicate with the Department of Neuropsychiatry, Michael Reese Hospital, 2908 Ellis Avenue, Chicago.

THE AMERICAN BOARD OF NEUROLOGICAL SURGERY

At a meeting of the American Board of Neurological Surgery, Chicago, Feb. 15 and 16, 1943, the following candidates passed the examination:

Samuel S. Allen, 3700 Fifth Ave., Pittsburgh; Capt. William F. Beswick, Medical Corps, Army of the United Staees; * Capt. Howard A. Black, Medical Corps, Army of the United States; Floyd H. Bragdon, Mercy Hospital, Pittsburgh; Bernard S. Brody, 107 Whitney Ave., New Haven, Conn.; Major Fritz Cramer, Medical Corps, Army of the United States; * Raymond M. P. Donaghy, Massachusetts General Hospital, Boston; Frederick A. Fender, 2361 Clay St., San Francisco; Harry E. LeFever, 9 Buttles Ave., Columbus; * Frank E. Polmeteer, Mayo Clinic, Rochester, Minn.; James L. Poppen, 605 Commonwealth Ave., Boston; Lieut. Comdr. Robert H. Pudenz (MC),U.S.N.; * Lieut. Theodore B. Rasmussen, Medical Corps, Army of the United States; * Charles Robert Watson, 1014 Doaghey Bldg., Little Rock, Ark.; * Capt. Thomas A. Weaver, Medical Corps, Army of the United States; * John E. Webster, 840 David Whitney Bldg., Detroit; Major Barnes Woodhall, Medical Corps, Army of the United States, and Ward W. Woods, University Hospital, Ann Arbor, Mich.

* Certificates will be issued after fulfilment of a two year practice requirement.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

SOME OBSERVATIONS ON EARLY HUMAN FETAL MOVEMENTS. JAMES E. FITZGERALD and WILLIAM F. WINDLE, J. Comp. Neurol. **76**:159 (Feb.) 1942.

Fitzgerald and Windle studied 15 human fetuses between 7 and 9 weeks of gestation (18 to 26 mm. crown-rump length) under various operating conditions. Regardless of the type or strength of stimuli used, no fetal movements of a reflex nature could be elicited from the 6 specimens during a general anesthetic, after preoperative administration of morphine or after injection of solution of posterior pituitary U. S. P., or from the 6 fetuses delivered after procaine anesthesia, preceded by morphine or solution of posterior pituitary. Three specimens observed at operations performed with the mother under spinal anesthesia and with no preoperative medication reacted to appropriate stimulation. Continuous motion picture records of the experiments were made. The estimated age of the responding fetuses was 54 to 58 days (22.5 to 26 mm. crown-rump length). The responses were of two types. While the fetus was receiving oxygenated blood the excitability was high. After anoxia had set in a lateral movement of the head and trunk followed stimulation of the parts of the face supplied by the fifth nerve. The fetal muscles retained excitability long after all reflexes had disappeared.

ADDISON, Philadelphia.

SOME CONSIDERATIONS OF THE ELECTROENCEPHALOGRAM IN THE "CONVULSIVE STATE." B. L. PACELLA and S. E. BARRERA, J. Nerv. & Ment. Dis. **96**:125 (Aug.) 1942.

In all studies of the electroencephalographic changes associated with convulsive shock therapy produced either by metrazol or by the electric current the development of slow, 2 to 4 cycle per second waves of moderate to high voltage, appearing either at random or in a continuous series for interrupted periods, have been described. The persistence of abnormal records of this type, which closely resembled those seen in the cryptogenic convulsive states, depended roughly on the number of treatments the patient had received. None of the patients showed a pathologic record prior to therapy; in none was there a family history of epilepsy, and in no case was there any semblance of a petit mal attack occurring at the time the abnormal potentials were being recorded. Thus, the "paroxysmal cerebral dysrhythmia" can be considered as directly attributable to the shock treatment and as due either to the passage of the electric current through the brain or to the changes associated with the convulsion itself. The evidence favors the latter hypothesis and raises the question whether the pathologic electroencephalogram observed in cases of epilepsy can also be considered as due to changes induced by the convulsion itself, rather than to the etiologic factors in the disease. However, the occurrence of pathologic brain waves in relatives of epileptic persons, as well as in patients suffering only from petit mal attacks, is against this view. The assumption that a hyperirritable cortex in epileptic patients is revealed by the electroencephalogram is not supported by the fact that a higher voltage is usually necessary to produce a generalized convulsion in successive treatments by electric shock. Also, in 6 epileptic patients experimentally subjected to electric shock, the voltage necessary to produce a generalized convulsion was within the same range as that required for psychiatric patients with a normal pretreatment electroencephalogram. It was noted, however, that after one electrically produced convulsion each of the epileptic patients

exhibited an increased incidence of grand mal and petit mal seizures in the next few days. Thus, the possibility of altering "latent epilepsy" to clinically manifest epilepsy by shock treatment must be considered.

CHODOFF, Langley Field, Va.

CHANGES IN NORMAL ELECTROENCEPHALOGRAM OF MACACA MULATTA WITH GROWTH. MARGARET A. KENNARD and LESLIE F. NIMS, J. Neurophysiol. **5**:325 (Sept.) 1942.

In the infant monkey cortical potentials began to develop at or before birth but were not well demarcated until three or four weeks after birth. From that time until the end of the sixth month there were progressive development and elaboration of the electroencephalogram until it resembled that of the adult. Frequency of waves was about 2 to 3 per second immediately after birth and increased to about 7 to 8 per second during the first six months and then slowly to about 10 to 12 per second by the end of the second year. The amplitude was low at birth, increased during the first six months and then slightly decreased. During the growth period the electroencephalogram became at once more complex and more uniform. There were less variations in the base line and in the type of potential. The effect of sleep could be detected in the older animals, but in the newborn infant fluctuations in the state of waking or sleeping were too slight and gradual to be correlated with the marked fluctuations in the type of the electroencephalogram, which may, however, be related.

The changes in the development of the infant monkey were like those described for man and were, as far as was known, coincident with the anatomic and functional development of the cerebral cortex.

ALPERS, Philadelphia.

EFFECT ON ELECTROENCEPHALOGRAM OF LESIONS OF CEREBRAL CORTEX AND BASAL GANGLIA IN MACACA MULATTA. MARGARET A. KENNARD and LESLIE F. NIMS, J. Neurophysiol. **5**:335 (Sept.) 1942.

Lesions were made in the cerebral cortex and the basal ganglia of 41 monkeys, and electroencephalograms were recorded before and after operation. In every instance there was a temporary change in the electroencephalogram which appeared during the first or second postoperative day and consisted of flattening and slowing of the waves of medium frequency. The change was transient, was independent of the specific area injured but was more pronounced after larger lesions. In acute experiments with the animal under dial anesthesia, lesions of the cortex or of the basal ganglia produced no change in the electroencephalogram. After lesions restricted to the cerebral cortex there was no significant change in the electroencephalogram except the transient one already described. There was no focal effect of lesions of the cortex, and usually none following combined lesions of the cortex and the basal ganglia. In a few instances focal epilepsy could be observed. A lesion of the head of the caudate nucleus or of the putamen or of both was followed by pronounced changes in the pattern of cortical potentials. Hypersynchrony of the 8 to 10 per second waves became intensified, and the 15 to 20 per second waves became less evident or vanished. Combined lesions of the motor areas of the cortex and the basal ganglia caused the most decided changes. Hypersynchrony appeared and persisted for as long as two years. True epilepsy, evident both clinically and in the electroencephalogram, was found in 5 out of 15 animals. All the lesions which caused alterations in the electroencephalogram produced the most extreme changes in those animals which had been operated on in infancy.

ALPERS, Philadelphia.

CEREBELLAR ACTION POTENTIALS IN RESPONSE TO STIMULATION OF PROPRIOCEPTORS AND EXTEROCEPTORS IN THE RAT. ROBERT S. DOW and ROBERT ANDERSON, J. Neurophysiol. **5**:363 (Sept.) 1942.

Cerebellar action potentials in the rat were recorded from surface folia after stimulation of exteroceptive receptors by moving the hair on different regions of

the animal's body and of proprioceptive receptors by tapping the tendons of isolated muscles of the forelimb and the hindlimb. The lobules explored were the highest part of the culmen, the lobulus simplex, the folium and tuber vermis, the pyramis, the uvula, crus I and crus II of the lobulus ansiformis and the lobulus paramedianus. Of the lobules explored the pyramis showed the most consistent activity after proprioceptive stimulation and the culmen after exteroceptive stimulation. There were marked differences in distribution of the responses, depending on which type of stimulation was used. Some of the potentials might have resulted from activity caused by intracerebellar connections. No consistent differences in the distribution of the responses were detected when different parts of the animal's body were stimulated. Because of the small size of the cerebellum, the rat was not the most suitable animal for this study. In respect to the cerebellar lobules activated, electrical stimulation of the sciatic nerve resembled exteroceptive stimulation more closely than proprioceptive stimulation. The distribution of activity throughout the cerebellum following electrical stimulation of the sciatic nerve in the rat was more widespread than in the cat, and much more so than in the monkey.

ALPERS, Philadelphia.

NEUROGENIC VESICAL DYSFUNCTION. C. E. JACOBSON JR., Proc. Staff Meet., Mayo Clin. **17**:286 (May 6) 1942.

Jacobson produced neurogenic vesical dysfunction experimentally in female dogs by section of the pelvic and hypogastric nerves, by differential section of the sacral nerve roots and by transection of the cauda equina and the spinal cord. "The changes occurring in vesical tone and vesical capacity were recorded by means of preoperative and postoperative cystometrograms while the concomitant changes in the upper part of the urinary tract were recorded by means of excretory and retrograde urograms. Alterations of the appearance of the bladder were noted by cystoscopic examination."

Three disinct types of neurogenic vesical dysfunction of the spinal cord were observed to occur as a result of experimental lesions involving the peripheral nerve supply of the bladder and the spinal cord. These were (1) the atonic bladder, (2) the autonomous bladder and (3) the automatic, or reflex, bladder.

The atonic bladder is characterized by decreased vesical tone, increased vesical capacity and the complete absence of signs of vesical contractions. Urographically, there may or may not be dilatation of the upper part of the urinary tract. Cystoscopically, the bladder appears to be dilated and to have thin walls, elongated ureteral orifices and a wide-gaping vesical neck. The atonic bladder probably develops as a result of chronic overdistention due to the loss of normal transmission of sensory impulses from the bladder to the spinal cord.

The autonomous bladder is characterized by increased vesical tone, decreased vesical capacity and the presence of autonomous vesical contractions. Urographically, there is usually dilatation of the upper part of the urinary tract. Cystoscopically, there is evidence of hypertrophy of the vesical mucosa and muscularis, as well as relaxation of the vesical neck. The autonomous bladder probably develops as a result of loss of the normal motor innervation, a loss which permits the intrinsic nerve plexus of the bladder to function independently of the nervous system.

The automatic, or reflex, bladder is characterized by increased vesical tone, decreased vesical capacity and the presence of automatic, or reflex, vesical contractions.

ALPERS, Philadelphia.

Neuropathology

PATHOLOGIC CHANGES IN THE BRAINS OF DOGS GIVEN REPEATED ELECTRICAL SHOCKS. KARL T. NEUBUERGER, RICHARD W. WHITEHEAD, ENID K. RUTLEDGE and F. G. EBAUGH, Am. J. M. Sc. **204**:381 (Sept.) 1942.

The authors induced convulsions in a series of 12 mongrel dogs by application of an alternating current. Shocks were applied at a potential of 80 volts and a current strength of 200 milliamperes; the duration of the individual shocks was

fifteen-hundredth second. Some of the animals died during the experiment. The others were killed by bleeding under anesthesia induced by soluble pentobarbital. The neuropathologic studies revealed that the cortex was more involved than the extracortical gray matter. The nerve cells showed rather widespread damage, including tigrolysis, paleness, swelling, vacuolation and in some instances even ischemic and "severe" changes. Satellitosis and neuronophagia were observed occasionally. Although the changes described in the brain are pathologic, they are not to be regarded as serious. Most of the nuclei of the nerve cells remained fairly well preserved. The variation in the degree of involvement may well be influenced by variation in individual susceptibility and by the degree of severity of the convulsions. The authors conclude that histologic changes induced by electrical shock in the brains of dogs are somewhat less severe than the changes observed after metrazol.

MICHAELS, Boston.

CEREBRAL LESIONS FOLLOWING ADMINISTRATION OF NEOARSPHENAMINE. CYRIL B. COURVILLE and CLEMSON MARSH, Arch. Dermat. & Syph. **46**:512 (Oct.) 1942.

Courville and Marsh report an unusual and hitherto unstudied lesion of the brain, which they designate as multiple symmetric foci of hemorrhagic necrosis, which constitutes an integral part of the encephalitis syndrome following intoxication with neoarsphenamine.

The lesion is closely allied to pericapillary encephalorrhagia in that it is composed of many perivascular hemorrhages, which in this case are grouped into circumscribed areas, in contrast to their otherwise diffuse spread throughout the white matter of the brain.

The basis for the study was a series of 12 cases of encephalitis due to arsphenamine in which the cerebral lesions were observed at autopsy. In 7 cases multiple symmetric foci of hemorrhagic necrosis were observed (in 1 case, both grouped and scattered petechial hemorrhages were present); in 4 other cases typical petechiae were scattered throughout the white matter, while in 1 case gross hemorrhage into the brain had taken place. Any combination of these three lesions may exist.

One feature of special interest was the tendency of the hemorrhagic foci to localize in regions of both the gray and the white matter of the brain. The corpus callosum, the optic thalami, the external capsule and the frontal and parieto-occipital centrums (forceps minor and forceps major) seem to be sites of predilection.

The further tendency of the lesion to occur in symmetric areas of the brain suggests some functional vascular basis for its occurrence. The focal blood vessels supplying these areas are evidently susceptible to the toxic agent to the same degree at the same time. While the lack of epinephrine may enter into this situation, as Ehrlich originally postulated, one can be more sure that dilatation of the blood vessels (arterioles) predisposes them to involvement by the toxic process.

Like disseminated petechial hemorrhages, the lesion is not necessarily fatal, as a case in which there was a rather long survival period indicates. although it must produce serious clinical residuals if at all widespread or severe.

The lesion should be considered a pathologic entity which with disseminated petechial hemorrhages and the rare gross cerebral hemorrhage constitutes one of the essential pathologic elements resulting in the clinical syndrome of post-arsphenamine hemorrhagic encephalitis. The occurrence of localizing or lateralizing clinical phenomena in a clinical case should suggest the occurrence of this lesion.

ALPERS, Philadelphia.

TRAUMATIC HEMORRHAGE INTO THE PITUITARY GLAND. R. A. MUNSLOW, J. L. HAYMOND and A. S. CRAWFORD, Arch. Path. **34**:431 (Aug.) 1942.

The authors report the case of a man aged 35 with a history of trauma to the head, followed by unconsciousness and death three and one-half hours later.

Autopsy revealed basal fractures of the skull with lacerations of both frontal and temporal lobes in their inferior portions. Scattered hemorrhages, measuring up to 6 mm. in diameter, were observed in the gray and white matter of the cerebrum, especially in the tegmentum pontis. Hemorrhages were seen also in the posterior lobe of the pituitary gland.

WINKELMAN, Philadelphia.

LISSAUER'S DEMENTIA PARALYTICA. A. J. GALBRAITH and A. MEYER, J. Neurol. & Psychiat. **5**:22 (Jan.-April) 1942.

Galbraith and Meyer report the case of a woman aged 40 who showed predominantly psychotic reactions for about six years before organic manifestations became apparent. The latter consisted of Argyll Robertson pupils, a Korsakoff-like syndrome and atypical serologic responses consisting in a negative Wassermann reaction and a colloidal gold curve characteristic of dementia paralytica. Examination elicited focal signs, such as left hemianopia, disturbance in visual attention, constructional apraxia, drawing disturbance, finger agnosia, inability to distinguish right and left, agraphia and acalculia. The signs pointed to lesions in the parieto-occipital region and suggested a diagnosis of Lissauer's dementia paralytica. This was confirmed by the pathoanatomic observations, which, though diffuse, were most intense in the occipital lobes. Here, in spite of absence of macroscopic atrophy, there were intense infiltrations, with invasion beyond the pia-glia membrane, disintegration of the cortical tissue, presence of numerous "plump" cells and foci of demyelination and unusually severe inflammation of the white matter. These changes are regarded by the authors as an early and "prespongiosus" phase of Lissauer's type, before atrophy or the status spongiosus, regarded as essential to this form, has developed. Pathogenetically, the case tends to confirm the original views of Lissauer and Alzheimer that the circumscribed lesions are the expression of a local intensification of the process and are not due to extraneous factors. The failure to demonstrate spirochetes in this and in other cases of Lissauer's form of dementia paralytica should not be regarded as absolute proof that spirochetosis is not responsible for the lesions.

N. MALAMUD, Ann Arbor, Mich.

OCULOLARYNGOPHARYNGOVELOPALATIVE MYOCLONIA IN A BULBOPONTILE SYNDROME. C. JAKOB and JUAN C. MONTANARO, Rev. neurol. de Buenos Aires **7**:85 (April-June) 1942.

Jakob and Montanaro give an account of a 35 year old man who suddenly was taken with a pain at the left angle of the mouth, was dizzy and vomited. Peripheral paralysis of the left side of the face and paresis of the right limbs developed rapidly. The patient was syphilitic. He was found on examination to have paresis of the left sixth nerve and paralysis of the left fifth and seventh nerves, right hemiparesis, anesthesia of the left side of the face and right hemihypesthesia. In addition, there was myoclonia of the palatal, pharyngeal, laryngeal and ocular muscles. He died about three years after the attack. Careful examination of the brain revealed a focus of degeneration in the left side of the tegmentum involving the nuclei of the cranial nerves from the fifth to the eighth. The fifth and seventh nerves were completely interrupted; the eighth, only partly. The following pathways were involved: the median and lateral fillets, the tract of Gowers, the central tegmental tract, the middle cerebellar peduncle and the greater part of the left reticular formation. The temporopontile and the pyramidal tracts were partially destroyed. In addition, the nuclei of the reticular formation, the superior olive, the cerebellar root of the vestibular nerve, the floccular peduncle in part and the mesencephalic root of the trigeminal nerve were destroyed. The authors conclude that velopalatine myoclonia is not due necessarily to a circumscribed focal lesion but is the functional result of an alteration of the total equilibrium of paleodentato-olivary systems.

BAILEY, Chicago.

PATHOGENESIS AND HISTOPATHOLOGY OF HYDROPHOBIA IN MAN. ISTVÁN TARISKA, Deutsche Ztschr. f. Nervenh. **152**:133 (May) 1941.

Tariska reports on the histologic changes in the brains of 2 children, each aged 9 years, who died of hydrophobia. In the first child the bite was on the left cheek; the patient received antirabic inoculations. Pathologically the case was characterized by severe inflammatory changes in the medulla and pons, with the greatest intensity of the reaction in the neighborhood of the hypoglossal nucleus. The inflammation was greater on the left side than on the right. The gasserian ganglion was involved on both sides, but the substantia nigra was unaffected.

In the second child the bite was on the right lower extremity; this child failed to receive antirabic inoculations. There were intensive changes in the intervertebral ganglia, the lumbosacral portion of the cord and the substantia nigra.

The author concludes that his cases do not support either the theory of Schaffer that the virus spreads through nerve pathways or the theory of Schükrü and Spatz that it is disseminated by way of the cerebrospinal fluid. He thinks it more likely that the virus spreads by way of the spinal ganglia and the sympathetic nerve chain.

MERRITT, Boston.

MICROGLIOMA. LADISLAUS BENEDEK and ADOLF JUBA, Deutsche Ztschr. f. Nervenh. **152**:159 (May) 1941.

Benedek and Juba report a case of a rare type of primary tumor of the brain, a microglioma. In a man aged 34 there developed over a span of four to five weeks headache, failing vision, aphasia, right hemiparesis and olfactory hallucinations. Examination revealed papilledema, amnestic aphasia and visual verbal agnosia and right hemiparesis, with increased reflexes and a Babinski sign. Necropsy revealed a large infiltrating, yellowish pink tumor of the left temporoparietal lobe. Histologically the tumor was very cellular and was composed principally of microglia cells, which stained specifically by Penfield's combined method. The only macroglia cells were in the white matter adjacent to the tumor. Connective tissue stains revealed a delicate mesh of reticulum, particularly around blood vessels.

It is the authors' contention that the tumor which they record was a true microglioma and that the microglia cells seen in the tumor were not scavenger cells in areas of necrosis. In support of this thesis are the facts that the microglia cells were the only elements present and that they were distributed evenly throughout the tumor, rather than around blood vessels and in necrotic tumor tissue.

ADAMS, Boston.

Psychiatry and Psychopathology

DETERIORATION OF PATIENTS WITH ORGANIC EPILEPSY. ALEX J. ARIEFF and G. K. YACORZYNSKI, J. Nerv. & Ment. Dis. **95**:49 (July) 1942.

Arieff and Yacorzynski studied 27 patients with organic epilepsy by means of the Stanford-Binet test over a period of several years to determine whether and to what extent deterioration occurs. The patients, who suffered from such conditions as craniocerebral trauma, infections, tumor, vascular disease and chronic alcoholism, were tested at intervals of one to nine years. As a group there was a decrease of 6 in the intelligence quotient between the first and the final test—a significant shift. A control group of epileptic patients without demonstrable cause for their seizures failed to show a general deterioration. In 37 per cent of the original group of patients there was a significant decrease in intelligence scores, in contrast to approximately 6 per cent of the control group who showed a decrease.

CHODOFF, Langley Field, Va.

THE PSYCHOPATHOLOGY OF THE EGO SYSTEM. GEORGE W. KISKER and GEORGE W. KNOX, J. Nerv. & Ment. Dis. **95**:66 (July) 1942.

Kisker and Knox undertake to apply the gestalt concept of the ego system to mental disorder. In gestalt psychology, the behavioral field is the field of experience or consciousness viewed in terms of dynamics or postulated forces. Mental development is the process of differentiation of the behavioral field from the state of homogeneity existing in infancy to a state of heterogeneity. The "things," or behavioral objects, which emerge in this process organize, influence each other and further articulate within themselves. The ego, as one of these objects, becomes abnormal if there is excessive or deficient ego emergence, ego articulation or ego relationship to other objects.

The ego, which is the most important part of the total field of experience, differs from the behavioral objects in that it serves as the axis and core of the behavioral field. The ego in its development goes through definite stages: (1) The "non-I" stage, in which the ego is at first undifferentiated from its environment; (2) the "I" stage, in which the ego later differentiates itself from its environment and articulates within itself; (3) the "my" stage, in which the ego incorporates other behavioral objects under its sphere of influence, and (4) the "we" stage, in which the ego becomes a subordinate of a larger group.

Mental abnormalities occur with various deviations from, or blocking of, these stages of ego development. These may take the form of regression to earlier stages, in which the individual becomes unable to distinguish himself from his surroundings. Splitting of the ego subsystems results in dual or multiple personality. If the ego is unstable or inadequate, it may attempt to achieve stability either by the expanding of material possessions or, if this is impossible, because of constraining geographic situation, by constructing an expanded framework for the ego system, with resulting grandiose delusions. The first type of reaction produces a dictator and the second a psychotic person, but there is no real difference between them.

CHODOFF, Langley Field, Va.

ON THE FEAR OF BEING BURIED ALIVE. SANDOR FELDMAN, Psychiatric Quart. **16**:641 (Oct.) 1942.

The idea "What if I should be buried alive?" is of great importance to both children and adults and occurs frequently. It creates depression, distracts attention from the social tasks of life and may arrest physical and mental development. It is often the sole cause of night terrors. It disturbs sleep.

In adults, the obsessional idea makes an indelible impression on the whole personality, disturbing normal activity and leading to compensations and reactions against the dreaded possibility. It may appear in the fantasies of early childhood. The whole waking life is obsessed with the fear, but it usually takes possession of the mind at night when the sufferer goes to bed.

In some cases moral discontentment was found to be responsible. A person is "dead" although physically alive if he cannot respect himself; he is "buried alive" if he cannot live up to his moral and ethical ideals. The author also presents evidence to show that the obsessional idea may be a desire on the person's part to be buried alive and to be dug out of the grave in order to have reunion with his parents.

In everyday language the expression is often heard and used, "You do not exist for me," "you are a dead man for me," if a person feels resentful and threatens another with the withdrawal of love. When a person is not loved by a dear one, when he does not count, he feels as if he were dead.

Not to be loved or not to love is expressed by the fear of being buried alive. It explains also the fear of death itself. Only he who loves and is loved feels he is alive and is not concerned with death. Not thinking of death, he is not afraid of it, even in old age. As is well known, the desire to repeat the experience of being in the mother, in the womb, where he was buried alive and yet connected

with the world and taken care of, also returns regressively in the fear of being buried alive and in the fantasy of arranging some kind of communication with the loved ones while alive in the ground.

LESKO, Bridgeport, Conn.

THE SUCCESSFUL TREATMENT OF A CASE OF ACUTE HYSTERICAL DEPRESSION BY A RETURN UNDER HYPNOSIS TO A CRITICAL PHASE OF CHILDHOOD. MILTON H. ERICKSON and LAWRENCE S. KUBIE, Psychoanalyt. Quart. **10**: 583, 1941.

In a woman aged 23 there suddenly developed a rapidly progressive and deepening depression. Both extrainstitutional psychiatric treatment and psychoanalysis were tried, but no improvement was obtained. Her friends reported that she was raised in a very moralistic family. When she was 13 years old her mother died. At 20 years of age she and her best friend fell in love with the same man, who married her friend. The next year the friend died, after which the man returned and renewed his acquaintance with the patient. After a date with him she returned depressed, disgusted and nauseated. From that point her illness began. The man stated that he had proposed marriage; she had accepted, but when he was about to kiss her she vomited over him.

As any approach by psychiatric or psychoanalytic technics had failed, and as these attempts had made her worse, it was decided to try hypnosis. The approach had to be indirect, for it was feared that the results of a direct approach might be serious. An arrangement was made to have her attend as a chaperone the hypnotic treatment of a friend. She was hypnotized without her knowledge. At the first session she was induced actually to regress to an age between 11 and 13 years and to report her mother's restrictive advice about sexual matters. With this advice the therapeutist agreed, simply raising the question whether the mother would not have instructed her further as she grew older. At the second session the events of the previous session were reviewed silently by the patient and then reported. It was again brought to her attention that her mother had died before she had a chance to finish her sexual instruction. At the third session the patient was told to repress all memories of the other sessions except the first posthypnotic story of her mother's sex instructions. Then both while she was under hypnosis and after hypnosis she was asked to consider what she thought her mother's further instructions would have been had she lived. This treatment resulted in a complete cure, with a change in her attitude toward men and ability to have dates and to marry the widower. Two years later she was still well and was happy with her husband and baby.

The procedure in this case was interesting. The therapeutist agreed with the patient's oversevere superego and modified it only in the light of growth from childhood to adulthood. The therapeutist also ordered the patient to suppress all but the most rudimentary insight. Treatment was started in an indirect way. The authors mention a number of questions raised by the case and the possibility in some cases of altering rigid psychoanalytic technic along similar lines.

PEARSON, Philadelphia.

A STUDY OF STRUCTURAL AND INSTINCTUAL CONFLICTS IN CASES OF HAY FEVER. G. W. WILSON, Psychosom. Med. **3**:51 (Jan.) 1941.

Wilson discusses the significance of material obtained from the psychoanalytic study of 7 cases of hay fever. He concludes that the psychogenic aspect of hay fever is a result of unsuccessful olfactory repression. Frustrated sexual curiosity early in life seems to be a primary factor in producing this unsatisfactory repression, with resultant displacement of interest to the physiologic function of elimination. All the patients in the series recalled childhood seductive experiences involving parental interest in excrement. Sensitivity to odors indicative of relatively increased olfactory perception was elicited in all patients. The dreams of 1 patient demonstrated the displacement of sexual curiosity and affective interest from the visual to the olfactory sphere. The author believes that unsatisfied olfactory sexual curiosity may be considered as a constant irritant to the nasal

mucous membrane. This internal psychogenic factor may be more or less important than the external pollen factor in various patients, and either may be sufficient to precipitate an attack of rhinitis. SCHLEZINGER, Philadelphia.

ALCOHOLISM AND MENTAL DISORDER. JACKSON M. THOMAS, Quart. J. Stud. on Alcohol **3**:65, 1942.

Thomas reports 5 cases to illustrate the multiplicity of factors which may be involved in the genesis of alcoholism. Many of the statistics in the past have ignored the complexity of the question and reflect largely the personal bias of the investigators. No general formula fits all cases, and each patient must be regarded as an individual problem who uses alcohol in his own peculiar way to assist in his efforts to adjust in life. Likewise, the more or less direct results from the use of alcohol vary greatly in different persons and under different circumstances. DRAYER, Philadelphia.

THE APPLICATION OF THE RORSCHACH TEST TO A SAMOAN GROUP. P. H. COOK, Rorschach Research Exchange **6**:51 (April) 1942.

The subjects were 50 students from a mission high school, where boys are trained to become native pastors. The mean age was 20.6 years. Though these boys may not be representative of true Samoans, they represent a genuine non-European cultural and racial group. All the boys came from the higher-ranking families and were above the average Samoan in ability and development.

The tests were given in Samoan by an interpreter. The primary purpose was to see how a non-European cultural group reacted to the Rorschach test and what could be elicited from such a group on the basis of the Rorschach theory. A few of the results follow: There was overemphasis on whole responses, which were simple and crude. The author feels that this manner of approach may be explained by the fact that the language and the level of development of the Samoan social pattern are far below that of other Rorschach subjects. Also, the Samoan's ambition exceeds his ability.

There was a large usage of white space (S). The reason for this, the author explained, may be the strong influence of the missions and the white men on these particular Samoans. Few determinants other than form (F) were used. Although this is usually a sign of a compulsive or depressive rigidity, here it might be due to the fact that the Samoans expect and accept a certain form of rigidity and compulsion. M responses were few, the FM type being used twice as often as the M type. In Samoans this does not necessarily mean emotional immaturity. To the Samoans, belief in spirits and a fear and anxiety for certain things are natural. Therefore the large use of k, K and FK responses is not startling. The small number of texture responses may be attributed to the lack of differentiation in personality and perception, as well as to an unfamiliarity with most objects referred to in common texture responses, such as "fur" and "rug." CF and pure C responses were much greater than FC responses, which may be explained, the author states, by the fact that the colors of the tropics are simple and harsh and the Samoans have developed little sensitiveness to color nuances. Although the choice of content was limited and stereotyped, there are two explanations for this: First, in intelligence the Samoan group would fall below an average American group; second, the opportunity for development is limited in the tropics. When voting for the most and the least preferred cards, the colored cards were the most preferred and card V was the least preferred.

A comparison of the differential data on the subjects, as presented by the schoolmasters, with the results of the Rorschach test were not satisfactory, primarily because the data given on the subjects were influenced by the preferences of the teachers and were not, therefore, altogether true. However, the Rorschach test can and should be applied to non-European cultural groups.

MARCOVITZ, Philadelphia.

Diseases of the Brain

THE INHERITANCE OF DIABETES INSIPIDUS. HARRY BLOTNER, Am. J. M. Sc. **204**:261 (Aug.) 1942.

Blotner reports a case of diabetes insipidus in a man whom he had observed for five years; the mother and grandmother also suffered from the disease. The patient was 25 years old and unmarried. As soon as he could walk and reach for water, it was noticed that he drank all that he could get. As he grew older, he imbibed as much as 3 or 4 gallons (11 or 15 liters) of water a day. His daily fluid intake and output had been about 10 to 12 liters. Solution of posterior pituitary U. S. P. administered intramuscularly or intranasally reduced the polyuria and polydipsia to normal. The patient's mother, a widow aged 50, had consumed much water since childhood, and up to the age of 10 years she always took a quart (946 cc.) or more to bed with her. The condition improved at the time of her menopause, and she takes now about 5 to 6 liters of fluids daily. The grandmother imbibed 2 gallons (7.5 liters) of water a day when she was a girl. She, too, improved at the time of her menopause but still had polyuria and polydipsia at the age of 64, when she died of heart disease.

The records of 70 patients revealed only these instances of familial diabetes insipidus. The disease may be inherited through the maternal or the paternal side and transmitted either to male or to female children. There is general impression that familial diabetes insipidus is due to a dominant gene.

MICHAELS, Boston.

NARCOLEPSY. HENRY G. HADLEY, J. Nerv. & Ment. Dis. **95**:13 (July) 1942.

Narcolepsy is characterized by attacks of untimely sleep and by cataplexy. Cataplectic attacks are due to cortical inhibition, and Pavlov expressed the belief that narcolepsy is due to excessive inhibitability of the cerebral cortex. Narcolepsy may be a manifestation of disease of the infundibular system, and Redlich has pointed out the frequent association of endocrine dysfunction with the syndrome. The symptomatic forms are without cataplectic manifestations, while the primary type shows both features of the syndrome and is of cortical origin. The symptomatic type may appear in cases of epidemic encephalitic, cerebral trauma, tumors of the floor of the third ventricle and the aqueduct of Sylvius, multiple sclerosis, dementia paralytica and epilepsy. Hadley reports a case of primary narcolepsy with the later incidental development of a glioma.

CHODOFF, Langley Field, Va.

EARLY SYMPTOMS OF APHASIA WITH BRAIN TUMORS. MARK KANZER, J. Nerv. & Ment. Dis. **95**:702 (June) 1942.

Kanzer believes that in cases of aphasia associated with tumor of the brain the initial manifestation is likely to be difficulty in word finding. There has been considerable controversy in the literature as to whether amnesic aphasia represents a special type or a variation of other types of aphasia which may occur with a number of diffuse and local lesions of the brain. Weisenburg placed amnesic aphasia in a special category because of psychologic differences from the other types of aphasia. His 5 cases were observed only in patients suffering from brain tumor. He made no suggestions as to the localizing value of amnesic aphasia.

The studies of Head included 5 cases of nominal aphasia, a term which undoubtedly corresponds to amnesic aphasia. All occurred in association with a mild cerebral lesion or during recovery from a more serious disorder.

Goldstein, who was concerned chiefly with the psychologic aspects of the disorder, expressed the belief that the diagnosis should be made only after detailed psychologic studies.

The author draws the following conclusions from the observations of the aforementioned investigators: 1. Amnesic aphasia is a mild disorder of speech, usually occurring in association with moderate trauma to the skull, during the early

stages of a tumor or during recovery from a vascular lesion or wound. 2. Pathologic studies have not yielded a clear conception of the localizing significance of the disorder. 3. Establishment of psychologic criteria for the diagnosis of amnesic aphasia has not led to a better understanding of its clinicopathologic background.

The author then turns to his own case material and states that the anamnesis usually reveals a characteristic picture marked first by "slight forgetfulness," which on close analysis is resolved into difficulty in using proper names or words as names of objects. When the patient is admitted to the hospital, examination usually gives the picture of a more advanced defect, in which the difficulty in naming objects appears to be part of a subtle, but more profound, intellectual and personality disturbance. In some cases the speech difficulties have gone beyond the stage of pure amnesic defect and there is an admixture with the signs of early sensory aphasia.

The localizing value of amnesic aphasia has been the subject of much debate. It remains inconclusive in spite of the claims of Kleist that the disturbance is associated exclusively with a lesion of the posterior part of the second and third temporal convolutions. The author believes, with Henschen, that amnesic aphasia may occur as an early symptom with lesions of various portions of the brain and that it represents a mild manifestation of true aphasia in the sense of Goldstein.

The author divides his cases into two groups: (*a*) those in which the aphasia appeared simultaneously with, or after, involvement of the right upper extremity and (*b*) those in which the occurrence of amnesic aphasia preceded the involvement of the right upper extremity. In the first group the lesion is believed to be anterior, the defect being akin to the early stages of typical Broca's aphasia, while in the second group the region of the posterior temporal and the parietal lobe is involved.

Two alternative theories are offered to account for these observations: 1. Amnesic aphasia may be regarded as a disturbance in language which is produced by disruption of the association pathways between the sensory and the motor centers of speech. 2. Amnesic aphasia may be considered as the result of an early lesion involving an extensive common language zone about the fissure of Sylvius, with loss of association functions.

CHODOFF, Langley Field, Va.

TRIGEMINAL NEURALGIA AND TUMORS OF THE GASSERIAN GANGLION. J. G. LOVE and H. W. WOLTMAN, Proc. Staff Meet., Mayo Clin. **17**:490 (Sept. 9) 1942.

Love and Woltman report 2 cases of tumor of the gasserian ganglion occurring in patients suspected of having typical trigeminal neuralgia. They comment on the rarity of tumors of the gasserian ganglion and call attention to the fact that in cases of trigeminal neuralgia with lack of freedom from pain between paroxysms tumor of the gasserian ganglion should be suspected.

ALPERS, Philadelphia.

HEREDODEGENERATIVE CEREBELLAR DISORDERS. ANTONIO R. DE MELLO, Arch. brasil. de med. **32**:109 (April) 1942.

After a brief history of the development of the present concept of the hereditary cerebellar disorders, Mello describes a case which he had the opportunity of studying clinically and pathologically. The observation concerns a woman whose disease began at about 29 years of age with unsteadiness of gait, which steadily progressed. Examination two months before death, at the age of 36, disclosed fixed facies, apathy, exophthalmos, slight ptosis, inability to walk, general muscular weakness and atrophy, especially in the distal parts of the lower extremities, slight asynergy on voluntary movement of the arms, a bilateral Babinski sign, exaggerated patellar reflexes and incontinence of feces and urine. The patient could scarcely speak even a few syllables and had great difficulty in swallowing.

She died of pneumonia. Several members of the family, representing at least three generations, had a similar complaint. Anatomic study revealed atrophy of the cerebellar cortex and sclerosis of the cerebellar tracts, the pyramidal tracts and the fasciculi of Goll.

The author offers this case in support of Austregesilo's thesis of the close relationship of Marie's cerebellar ataxia, Friedreich's ataxia and peroneal atrophy. He proposes to call the condition in his case spinocerebellar heredoataxia.

BAILEY, Chicago.

Treatment, Neurosurgery

AN ANALYSIS OF DEATHS FOLLOWING THERAPEUTIC MALARIA. UDO J. WILE and LESLIE K. MUNDT, Am. J. Syph., Gonor. & Ven. Dis. **26**:181 (March) 1942.

Since 1925, 1,026 patients with neurosyphilis have been treated by inoculation with malaria at the University of Michigan Hospital. Wile and Mundt report their analysis of the causes of the 29 deaths. They suggest, in retrospect, that some of the deaths might have been prevented. This is particularly true since the advent of sulfonamide therapy, which might have prevented some of the deaths caused by infection. Sixty-six per cent of the 29 deaths occurred in patients with dementia paralytica, the highest mortality rate occurring in the older age groups.

The most frequent serious complication responsible for 12 deaths was sudden peripheral circulatory failure or vascular collapse. The signs and symptoms were those of true medical shock. The time and occurrence of the circulatory collapse were unpredictable, coming on at any period during treatment. The deaths of 5 patients were attributed, directly or indirectly, to extreme hyperpyrexia; 5 patients died as a result of pneumonia, while intercurrent acute infection, vascular accidents, internal hemorrhage and suicide (in 2 cases) accounted for the death of the others.

BECK, Buffalo.

USE OF ALPHA TOCOPHEROL IN THE TREATMENT OF NEUROMUSCULAR DISORDERS. ALBERT J. LUBIN, Arch. Int. Med. **69**:836 (May) 1942.

Lubin reports on the use of alpha tocopherol in large doses in 35 cases of neuromuscular disorders. At frequent intervals the patient's subjective impressions and quantitative measurements of their progress were obtained. Muscular strength was measured by dynamometric methods. Electrical reactions to faradic and galvanic currents were noted, and chronaxias were measured. Frequent determinations of the creatinine and the creatine output in twenty-four hours were performed. The patients consisted of four groups: (1) 7 with amyotrophic lateral sclerosis; (2) 9 with muscular dystrophy; (3) 5 with muscular atrophy of unknown cause, and (4) 14 with other diseases of the neuromuscular system.

The condition of 31 patients remained stationery or became worse during the period of treatment. In the 4 patients who showed improvement it was shown that alpha tocopherol was in no way responsible for the beneficial results. The method of study is suggested for use of other investigators of the problem of neuromuscular disorders.

BECK, Buffalo.

WARD THERAPY. NATHAN BLACKMAN, Psychiatric Quart. **16**:660 (Oct.) 1942.

Blackman describes a method of group psychotherapy characterized by passive guidance on the part of the therapeutist and active participation by the patient. The atmosphere is one of friendliness and impartiality. The patients present their own cases, and instructive discussions by the patient and other patients and the therapeutist are held. This method of ward therapy is presented as a means of utilizing available psychiatric guidance in the face of an ever increasing scarcity of medical personnel.

LESKO, Bridgeport, Conn.

THE TREATMENT OF BRAIN ABSCESS. D. W. C. NORTHFIELD, J. Neurol. & Psychiat. **5**:1 (Jan.-April) 1942.

Northfield reviews his treatment of abscess of the brain in 31 patients and finds that of 12 patients treated by drainage only 3 lived, whereas of 19 patients treated by aspiration, decompression or enucleation alone or combined 11 survived. Thus closed methods of treatment offer a much more favorable prognosis than the open method. Failures are primarily due to such complications as multiple abscesses, massive edema or acute meningitis. Edema may be controlled in the early stages by dehydration therapy, but as a rule the best results are achieved by surgical decompression. When meningitis, including ventriculitis, is a complication of brain abscess it should be treated by decompression measures rather than by frequent lumbar punctures, since the latter tend to promote herniation. Chemotherapy doubtless combats meningitis, but not the abscess proper. Successful treatment depends on accurate localization and a diagnostic burr hole, tapping or ventriculography. The time of surgical intervention varies but should be resorted to whenever the clinical condition begins to deteriorate. Aspiration should be attempted first. This is followed by decompression only if tension is not sufficiently relieved, if there is considerable swelling of the brain or if the abscess is deep seated. At the time of aspiration, the cavity of the abscess should be irrigated with a 50 per cent electrolytic solution of sodium hypochlorite. Repeated aspirations may be necessary, but intervals will gradually lengthen. Injection of 1 to 2 cc. of thorium dioxide into the abscess may be of help in roentgenologic visualization of the organization of the wall of the abscess. Enucleation of an abscess depends on the formation of a well defined and tough wall. This optimum period varies, but the usual time is about the third month. Enucleation may prevent the occurrence of a convulsive disorder, and anticonvulsants should always be administered until the abscess is fully eradicated. Drainage should be used only in exceptional cases, such as those of infected compound fractures of the skull or superficial subdural abscess.

N. MALAMUD, Ann Arbor, Mich.

Encephalography, Ventriculography, Roentgenography

THE SIGNIFICANCE OF VERTEBRAL FRACTURES AS A COMPLICATION OF METRAZOL THERAPY. NORMAN L. EASTON and JOSEPH SOMMERS, Am. J. Psychiat. **98**: 538 (Jan.) 1942.

Easton and Sommers studied the incidence of vertebral fractures in 200 patients both before and after metrazol therapy. They found a fracture incidence of 23 per cent, with a slightly greater frequency in males than in females. Age was a factor, since the fewest fractures occurred between the ages of 21 and 55, and the highest incidence occurred after the age of 55. The average number of vertebral fractures per patient was 2.4. All fractures occurred in the thoracic region, the greatest number involving the fourth, fifth and sixth thoracic vertebrae. All were confined to the bodies of the vertebrae, chiefly to the superior portion. In no case were the laminas or pedicles involved. Pretherapy roentgenograms in some cases showed kyphosis, scoliosis, arthritis, nuclear changes or old fractures. None of these conditions predisposed to the development of vertebral fractures. Roentgenographic examinations and determinations of calcium of the blood and spinal fluid carried out through the course of metrazol therapy gave no indication of a specific effect of metrazol on calcium metabolism. Moreover, no correlation between the mental status and the incidence of fractures could be determined. Easton and Sommers comment on the mild nature of the symptoms resulting from the fractures. Less than half of their patients complained of pain, and only 3 of the patients had recurrence of pain. The authors state that the most important aspect of therapy is prophylactic and recommend mechanical support of the spine during convulsions.

FORSTER, Boston.

ACQUIRED SUBTENTORIAL PRESSURE DIVERTICULUM OF A CEREBRAL LATERAL VENTRICLE. CORNELIUS G. DYKE, Radiology **39**:167 (Aug.) 1942.

Dyke states that no cases of the condition which he describes have been recorded in the literature, though there are numerous reports of cerebral defects due to other disturbances. An acquired subtentorial pressure diverticulum of a cerebral lateral ventricle is a condition in which part of the medial portion of a lateral ventricle extends medially and caudally through the tentorial incisura to exist as an accessory infratentorial, fluid-filled sac. It is important that this be recognized and that the diverticulum be not confused with a rostrally displaced fourth ventricle.

Three cases of the lesion are cited, 1 of which was verified at necropsy. The diagnosis was made in 2 instances from the pneumencephalograms. The first case was that of a young man who had had attacks of unconsciousness for five months. Roentgenograms of the skull showed a decided increase in intracranial pressure. Pneumencephalograms revealed conspicuous enlargement of the lateral and third ventricles and an unusually large collection of gas beneath the tentorium, which at necropsy proved to be a diverticulum of the left lateral ventricle. Case 2 was that of a woman aged 46, who had had paresthesias of the left side of the face and body for five years and sudden temporary paralysis of the left side of the body. Ventriculograms showed notable ventral depression of the lateral ventricles and a large collection of gas beneath the tentorium which undoubtedly represented a pressure diverticulum of the lateral ventricle. Case 3 was that of a 16 year old girl who complained of "loss of pep," headache, amenorrhea and diplopia. Great dilatation of the lateral and third ventricles and a moderate-sized diverticulum were demonstrated on ventriculographic examination. It is interesting to note that the author demonstrated the diverticulum in 2 of the cases by laminagraphic studies of the air-filled ventricle.

The diagnosis of the condition is important, as the size and shape of the diverticulum are not unlike those of a greatly dilated fourth ventricle. It usually occupies a position too high for the fourth ventricle and in most cases is much larger than this structure.

The portion of the medial wall of the lateral ventricle to give way was apparently the hippocampal gyrus. The distance which the medial wall of the ventricle must migrate to reach the edge of the tentorium is negligible, for normally the medial margin of the atrium and the posterior third of the body of the lateral ventricle are practically in the same vertical plane as the free edge of the tentorium. This is true of the exact area where the hippocampus swings laterally from the thalamus, and the gyrus here is rather thin. Therefore when the lateral ventricles are enlarged, particularly when they are greatly dilated, the medial portion of the atrium of the lateral ventricle is actually medial to the free edge of the tentorium, thereby facilitating the formation of a subtentorial diverticulum.

The underlying cause of the subtentorial diverticulum in all the cases was pronounced elevation of the intracranial, especially the intraventricular, pressure. The nature of the wall of the diverticulum cannot be determined, but there is probably a thin layer of brain tissue and leptomeninges and the wall may well be lined with ependyma.

KENNEDY, Philadelphia.

THE ROENTGENOGRAPHIC APPEARANCE OF THE BONES IN CUSHING'S SYNDROME. MARCY L. SUSSMAN and BENJAMIN COPLEMAN, Radiology **39**:288 (Sept.) 1942.

The clinical picture of Cushing's syndrome in the female, in whom most of the cases have been reported, consists of deposition of fat on the trunk, vascular hypertension, amenorrhea, purplish striae on the abdomen and thighs, choleric facies, various degrees of hirsutism, actiniform eruptions, decreased sugar tolerance and osteoporosis. The syndrome apparently occurs with basophilic adenoma of the pituitary gland and tumors of the adrenal cortex, and rarely of the thymus, or without tumor of any of these organs. The association of a tumor with Cushing's syndrome occurs rarely in the adult male, regularly in the child and commonly

in the adult female. In all cases the basophilic cells show characteristic hyaline changes; it may be, however, that the hyalinization represents a period of overactivity of the basophils as a consequence of inactivation of certain subsidiary ductless glands.

There are a decrease in the estrogens of the blood and an increase in the androgens. Androgens may inhibit the effect of the estrogens on the formation of bone, which may account for the severity of the osteoporosis. The most important factor, however, is thought to be a negative nitrogen balance due to the increased conversion of proteins into sugars.

Osteoporosis is of common occurrence in cases of Cushing's syndrome. Eisenhardt and Thompson found that of 61 patients, ranging in age from 11 to 78 years, 53 had definite osteoporosis, 5 showed questionable changes and 3 had normal bones. In the authors' series of 7 patients, from 19 to 49 years of age, 6 had osteoporosis. The skull was most often involved, but the more striking changes were noted in the ribs and spine. In 1 patient the long bones were involved.

The osteoporosis of the skull, seen in 5 of the 7 patients, was irregular in distribution and occurred most often in the frontal and parietal regions. The areas affected were irregularly triangular or ameboid, with poorly defined margins, or were roughly circular, resembling metastatic carcinoma. In 1 patient the skull showed diffuse coarsely granular mottling. Occasionally only the dorsum sellae was osteoporotic.

The spine revealed uniform osteoporosis, this being found in all segments. The bones were more radiolucent because of a uniform decrease in the number and density of the trabeculae. The osteoporosis may be severe, resulting in compression fractures of the vertebrae, or may be so mild that it is difficult to recognize. It has no specific characteristics.

The ribs show a peculiar change near the costochondral junctions which is almost pathognomonic. It is usually found in the lower ribs and is symmetric as a rule. The ribs are expanded to about twice their normal size for a distance of about 1 inch (2.5 cm.). The area is sharply outlined, as though by a calcified shell. Within this the deposit of calcium is uniform and homogeneous. The affected areas are denser than the surrounding bone, their appearance suggesting callus formation. No fracture line was visible in the present series of cases, although it has been reported. The histologic picture was indistinguishable from callus. Fractures of the vertebral bodies are readily explained as a result of loss of strength due to the osteoporosis. This may also explain the rib fractures, but it is significant that such fractures have not been reported in cases of osteoporosis occurring after the menopause or in association with nutritional disturbances. In Albright's cases of menopausal osteoporosis there was a history of fracture of ribs in only 1 instance.

In 1 case the osteoporosis was extreme, and the humeri and femurs were involved. The more profound changes occurred in the cases of adenoma. The duration of the illness could not be correlated with the severity of the changes observed in the bones. In all the cases there was a tumor of the adrenal cortex—in some a benign adenoma and in others a carcinoma. KENNEDY, Philadelphia.

Society Transactions

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

N. W. WINKELMAN, M.D., *President, in the Chair*

Annual Meeting, June 4, 1942

Miliary Aneurysms: Relation of Anomalies of the Circle of Willis to Formation of Aneurysms. DR. HELENA E. RIGGS and DR. C. RUPP, Philadelphia (by invitation).

A study of the circle of Willis in 1,437 consecutive cases demonstrated the presence of aneurysms measuring 0.5 cm. or less in 131 cases (9 per cent). In 28 cases multiple aneurysms were present, as many as 5 being noted in a single case. The absence of any significant increase in the number of these lesions in the older age groups largely eliminates systemic disease, such as arteriosclerosis or hypertension, as a primary etiologic factor. Failure to discover any aneurysms in a group of 102 infants and children under 10 years of age lends confirmation to the theory of Forbus that miliary aneurysms as such are not of congenital origin but that their development is fundamentally related to structural defects in the arterial wall of embryonic origin. The location of the aneurysms in this series of cases strengthens this hypothesis. All these lesions were located in relation to arterial branchings, areas in which, as Forbus has demonstrated, congenital structural defects of the arterial wall are characteristically present.

Site: Arterial Branching	No. of Cases
Anterior cerebral with anterior communicating artery	79
Middle cerebral with anterior cerebral artery	36
Internal carotid artery with:	34
Anterior communicating artery	
Anterior choroidal artery	
Basilar artery with:	15
Posterior communicating artery	
Superior cerebellar artery	
Posterior inferior cerebellar artery	
Vertebral artery	
Bifurcation of anterior cerebral artery (second portion)	6
Bifurcation of posterior cerebral artery	2

Forbus suggested that the evolution of aneurysms in such areas is affected largely by mechanical forces and that the high intravascular pressure normally developed at bifurcations, when exerted against the congenitally weak arterial wall in that area, provides the necessary mechanism by which the dilatation is effected. This hypothesis, however, does not account for the failure of aneurysms to develop at all bifurcations at which structural weakness of the wall is present. Further, such a theory is tenable only for the development of aneurysms from areas of structural weakness located at points where the parent stem divides into two branches of equal size. In this study only 26 per cent of the aneurysms occurring at arterial branchings were located at such bifurcations; 74 per cent occurred at the branching of a small artery from the side wall of a parent vessel of greater caliber.

The presence of a high degree of association of aneurysms and anomalies of the circle of Willis ($\chi^2 = 13$) in this series suggests that such structural mal-

formations, by producing local alterations in intravascular dynamics, may provide a mechanical basis for the development of aneurysm in congenitally weak portions of the vascular wall. Analysis of the location of the aneurysms in relation to abnormal formations of the circle of Willis demonstrates that 86 per cent of these lesions lay in fields where anomalies provided a potential source of hydraulic imbalance.

Sarcoma of the Temporal Lobe Associated with Abscess and Invading the Subcutaneous Extracranial Tissues. Dr. P. Bailey, Chicago.

History.—A white woman aged 40 was admitted with the complaint of headache of two months' duration. She had been well until March 1941, when she had a sore throat, from which she recovered promptly. In May 1941 severe generalized headaches began, the pain at first lasting a few days and gradually becoming continuous. She had vomited almost daily for the last three weeks.

Examination on July 14, 1941 showed bilateral papilledema of about 4 D. The visual fields were normal. Roentgenograms of the skull revealed irregularity of structure of the vertex, of questionable pathologic significance. The diagnosis was unlocalized intracranial lesion, probably glioblastoma, with hypertension. A ventriculogram, made on July 15, revealed evidence of a lesion in the right temporal area. A subtemporal decompression was made in this region, and from a cavity thin pink fluid was aspirated; microscopic examination of this fluid revealed no organisms and culture yielded only a few colonies of diphtheroids.

The patient slowly recovered from the operation. The wound gradually became more troublesome, however, and drainage yielded only a small amount of purulent material. The lesion was treated for many weeks with local applications of sulfonamide compounds, and, from July to December 1941, six operations were performed for revision of the abscess cavity, excision of cortex and débridement of an area of osteomyelitis involving the temporal, parietal and frontal bones. The edges of the wound became progressively thickened; in November left hemiparesis followed the débridement, and in December and January the patient received intermittent doses of roentgen rays, amounting to some 1,100 r in all. After the cessation of roentgen therapy, the piling up and thickening of the edges of the wound increased rapidly, and the lesion extended to the vertex of the skull and down the entire right side of the face, involving the face and the right eye in an indurated swelling. Various organisms, including Staphylococcus aureus, Streptococcus haemolyticus, Pseudomonas aeruginosa and Encapsulatus aerogenes, were isolated from the wound, which had by now closed to a narrow sinus. The patient became weaker and died April 10, 1942.

Autopsy.—Complete postmortem examination disclosed nothing of importance except for the cerebral lesions. The anterior part of the right temporal lobe of the brain was occupied by a firm, whitish mass, sharply demarcated from the brain tissue and continuous with the indurated subcutaneous tissue of the face and scalp. This tumor was only loosely adherent to the dura mater except around the decompression opening in the skull. Above the tumor, in the dorsal part of the temporal lobe, was the sinus track, with a small collection of pus at its inner extremity. The brain had herniated slightly around the drain. The ventricles were covered by a whitish granular material, which looked like the surface of a cauliflower.

Microscopic Examination.—The intracranial and the extracranial portion of the tumor, as well as the intraventricular nodules, were similar in structure. Broad, streaming bands of elongated cells formed a stroma which divided the neoplastic mass into alveoli. The nuclei of the neoplastic cells were chiefly oval and somewhat vesicular. Mitoses were numerous. Perdrau's method revealed an abundant network of reticulin, lying chiefly in the stroma but often permeating the tumor, in intimate association with the neoplastic cells. There could be

no doubt that the tumor was an alveolar sarcoma of leptomeningeal origin. There was also purulent infection of the brain, meninges and ventricular walls.

Comment.—It is unusual for an intracranial tumor to infiltrate the subcutaneous tissue in this manner. I have never known a glioma to do more than bulge outward through a decompression opening as a well circumscribed mass. Intracranial sarcoma is so rare that I have had no experience with extension into subcutaneous tissues by such a tumor. Is it possible that there was, nevertheless, an abscess and that the neoplasm was caused by the large quantities of a sulfonamide compound used in the wound? Such an explanation would account for the intracranial and the extracranial growth without the assumption that the intracranial tumor spread outward to invade the subcutaneous tissues. That there was a serious infection was proved by the development of osteomyelitis of the skull, but this may have been secondary. It is not likely that irritation from the long-standing infection could have given rise to the neoplasm; such an origin would be without precedent in my experience. Actually, it seems to me impossible to answer these questions.

DISCUSSION

DR. L. H. ZIEGLER, Wauwatosa, Wis.: Several years ago, a boy about 10 years old was referred to me because of headaches, vomiting and evidences of increased intracranial pressure. He had occasional slight fever, but no well defined localizing signs; however, one or two of the cranial nerves were partially palsied. A lumbar puncture, cautiously done, revealed a count of about 50 cells per cubic millimeter of spinal fluid. My associates and I were puzzled to know whether the condition was encephalitis or a neoplasm, but we favored the diagnosis of encephalitis. However, this was in the days before the advent of sulfonamide drugs. The process was progressive, and a subtemporal decompression revealed widespread sarcoma of the meninges. On the patient's death this diagnosis was verified. The sarcoma had in places invaded the brain, especially around blood vessels.

DR. R. B. RICHTER, Chicago: With regard to the experimental angle of the problem, the study by Haerem (*Proc. Soc. Exper. Biol. & Med.* **45**:536 [Nov.] 1940) is of interest. He observed in a tumor-free strain of mice that spindle cell sarcoma developed in 10 per cent of animals given subcutaneous injections of sulfanilamide in lard, while tumor did not appear in any of a large number of control animals given injections of lard alone.

Experimental Studies on Electric Shock Treatment: Intracerebral Vascular Reaction as an Indicator of the Path of the Current. DR. LEO ALEXANDER and DR. H. LOWENBACH, Durham, N. C.

In a previous study by Alexander and Weeks, it was observed that if an electric current of a magnitude sufficient to abolish irritability and conductivity of the nerve fiber was passed through a peripheral nerve, capillary and supracapillary anemia of the vascular bed established itself in that part of the nerve through which current had been flowing. This anemia lasted until shortly before irritability and conductivity of the nerve returned. More recently, Echlin produced localized cerebral anemia by direct electrical stimulation. While previous experimental work on electric shock, similar to that used in treatment, had tended to show rather diffuse cerebral and meningeal changes, not all of which were of clearcut pathologic significance, the observations by Alexander and Weeks make it appear extremely unlikely that electric current would distribute itself diffusely throughout the brain, but suggested the existence of a fairly clearcut path from one electrode to the other. Therefore, we felt that it was necessary to carry out experiments by which we could outline clearly the characteristic vascular reaction to the electric current.

With doses above the therapeutic level, with respect both to strength and to duration, we produced clearcut capillary and supracapillary anemia of what is morphologically the frontal lobe in the cat (i. e., the frontocruciate region) whenever the electrodes were applied in a way comparable to the usual method of producing electric shock in man—namely, with the current passing from the area in front of one ear to the area in front of the other, through electrodes measuring 100 sq. mm.

This supracapillary and capillary anemia of the frontal region, presumably caused by vasoconstriction as a consequence of the passage of the electric current, lasted up to one and one-half hours. With shock doses comparable to those used in treatment, the anemia (vasoconstriction) one-half hour after the shock was either slight or equivocal, or no change could be recognized at all. It is concluded that no consistent pathologic changes of any significance were caused by shock doses of electric current comparable to those used in treatment and that the fundamental changes caused by the electric shock treatment must be essentially physiologic or physicochemical.

DISCUSSION

Dr. L. Kalinowsky, Brentwood, N. Y.: There are available now several experimental studies in which the current was comparable in intensity and duration to currents used in treatment of human beings. Most of these studies did not reveal any important pathologic change in the brain tissue. The results of Dr. Alexander and Dr. Lowenbach are in full accord with the observations of Cerletti and Bini (*Riv. sper. di freniat.* **64**:1, 1940), with the recent studies of Moore and Winkelman and with the work of Barrera and myself. The only investigation in which different results were obtained is that of Alpers and Hughes, who observed numerous hemorrhages in their animals. In this connection, I wish to mention the work of Stender (*München. med. Wchnschr.* **84**:1893, 1937), who observed hemorrhages of the same type in animals after metrazol convulsions. He was impressed by the similarity of such hemorrhages to those in cases of concussion and suggested that they might be explained by injury to the head sustained during the violent convulsion. He therefore treated a second series, putting the animals in a padded box during the convulsions. In none of the animals of the second series were hemorrhages seen. This observation may be of possible aid in explanation of the variable results of studies on electric shock convulsions, all the more as Hassin did not see such hemorrhages in the brains of electrocuted criminals, to whom currents of intensities many times those employed in shock treatment were applied.

Dr. M. T. Moore, Philadelphia: Dr. Alexander's presentation has made clear two important facts regarding the effect of an electric current on the smaller vessels of the brain. First, currents of an intensity not in excess of that sufficient to produce a convulsion in the cat, analogous to that observed in human subjects, do not produce rhexis of the intracerebral or the meningeal vessels. Second, when a current of sufficient intensity to produce hemorrhages is used, the hemorrhages occur in the path of the electric current between the electrodes and are not diffusely scattered throughout the brain.

In several recent reports of convulsions experimentally produced by means of electric shock, subarachnoid and intracerebral hemorrhages of rather scattered distribution have been described. It is important, in the light of the evident efficacy of electric shock in the treatment of the affective psychoses, to evaluate these observations. In experiments with convulsions induced in cats, Dr. Winkelman and I have failed to find any evidence of cerebral hemorrhage, or indeed any change of note, when the animals were treated in a manner similar to that used with human beings. Some of the histopathologic changes reported may be attributed to factors other than the passage of the electric current alone. Neumann, Cohn and Katzenelbogen (*Am. J. Psychiat.* **98**:671 [March] 1942) observed cerebral changes in a controlled group of 7 cats, of which 3 were permitted to live for several months in the laboratory, 2 were killed shortly after arrival

and 2 died of "sniffles." Examination of the brains of these animals showed pyknosis and edema in 4, toxic encephalopathy in 1, congestion and stasis of the cerebral vessels in 3 and petechial hemorrhages in 2. We, likewise, have observed in control animals similar histopathologic changes, as well as fibrosis of the meninges. Ferraro and Roizin (*J. Neuropath. & Exper. Neurol.* **1**:81 [Jan.] 1942), in their work on acute experimental inanition in cats, showed, among other things, vascular changes varying from slight productive alterations to severe involvement, as well as occasional hemorrhages. Prados and Swank (Vascular and Interstitial Cell Changes in Thiamine-Deficient Animals, ARCH. NEUROL. & PSYCHIAT. **47**:626 [April] 1942) demonstrated that in animals with nutritional deficiency, particularly thiamine deprivation, vascular disturbances occurred in the brain, eventuating in petechial hemorrhages. The vascular changes consequent to thiamine deficiency have been stressed by Alexander and others. Alexander indicated that the vulnerability of the wall of the smaller vessels is influenced by such deficiency. In the experimental work of Alpers and Hughes (Changes in the Brain After Electrically Induced Convulsions in Cats, ARCH. NEUROL. & PSYCHIAT. **47**:385 [March] 1942), the first two groups of animals were treated with electric cerebral shock daily except on Sundays. Animals treated in such a manner often show a disinclination to eat, and it is quite possible that these animals suffered from nutritional deprivation. Treatments with the electric current were therefore an added disruptive factor, and it is not inconceivable that the vasculature predisposed to weakness by a vitamin deficiency may have given away, with resulting hemorrhages. It may be noted here that these hemorrhages were fairly widely distributed and did not correspond to the "track" hemorrhages, as illustrated by Dr. Alexander.

DR. N. W. WINKELMAN, Philadelphia: Dr. Alexander and Dr. Lowenbach have shown that with shock doses comparable to those used with human subjects the anemia in the brain one-half hour after the shock was either slight or absent, but with doses above the usual therapeutic level clearcut anemia was produced along the pathway of the current.

I wonder whether the authors studied the eyes of their experimental animals. In human subjects Dr. Moore and I have noted conspicuous congestion of the conjunctiva and sclera almost immediately after the application of the current. There appeared to be no preliminary vasoconstruction.

DR. LEO ALEXANDER, Durham, N. C.: I am grateful to all the discussers for their comments, and I am sure that with their joint efforts some light will be shed on the still unknown basic factors, physiologic, physical and chemical, which are operative in electric shock treatment.

Scarlatinal Encephalomyelitis. DR. N. W. WINKELMAN, Philadelphia.

In the perivenous, demyelinating form of encephalitis many etiologic factors are concerned, but for the most part the disease complicates vaccination and the acute infectious diseases of childhood, such as measles, chickenpox and smallpox, which attack the skin.

Because of the rarity of the encephalomyelitis during scarlet fever, the following case, in which the histopathologic changes conformed to the usual picture of so-called postvaccinal encephalitis, is reported.

In a 9 year old Negro girl signs and symptoms of diffuse involvement of the brain and spinal cord developed on the eighth day of her illness with scarlet fever. She died, with bulbar symptoms, in two days, after a stormy course.

Myelin sheath stains of the cortex, subcortex, basal ganglia, brain stem and spinal cord showed areas of demyelination, which were distributed almost entirely around the veins. Many of the smaller veins contained thrombi in various stages of organization. With cell stains the cortex for the most part revealed architectural disturbance as the result of mild loss of cells, increase in the macroglia and microglia and perivenous cuffing, made up of a narrow zone of hematogenous

elements (lymphocytes and plasma cells), surrounded at times by a wide band of microglia cells and phagocytes. The subarachnoid space was invaded only secondarily by a few inflammatory and phagocytic elements.

The changes in the subcortex were highly developed. There the perivenous involvement reached a maximum, with cuffing of the vessels by a few lymphocytes and plasma cells, intermingled with many phagocytes and microglia cells, the infiltration reaching far out into the tissues, without sharp delimitation. A generalized macroglial increase was present.

The changes in the brain stem were of a similar nature but of somewhat less pronounced degree. The perivascular accumulations showed fewer hematogenous cells, with microglia cells and phagocytes streaming out into the parenchymatous substance. The ganglion cells were spared in great measure, but they presented acute changes of various kinds.

The spinal cord showed changes similar to those of the rest of the central nervous system. Both the gray and the white matter were involved. Severe perivenous demyelination and cellular reaction, resembling the changes in the brain stem, were noted. The motor cells of the ventral horn were fewer, although normal cells could be seen. The membranes, especially those in relation to the anterior fissure, showed an inflammatory reaction. Marginal gliosis of severe degree bordered the anterior fissure but was less pronounced around the rest of the cord. The spinal ganglia were completely surrounded by hematogenous cells, together with some phagocytic elements. The ganglia themselves were not directly invaded by these elements.

The cerebellum showed changes of the same type as those noted in the rest of the central nervous system. Here, also, the white matter was chiefly affected.

This study, centered around a single case report, disclosed three important facts. 1. Unlike other exanthems, scarlet fever is rarely complicated by encephalomyelitis of the perivenous type. 2. The conclusion of Ferraro and Scheffer that the perivenous type of encephalomyelitis is not an inflammatory process in the strict sense of neuropathologic nomenclature, and that it should be termed an encephalopathy, is probably correct. 3. Perivenous encephalomyelitis usually occurs with acute exanthemas due to virus infection. Scarlatina, a streptococcic infection, is the exception to the rule. The histopathologic picture, however, conforms to that of postvaccinal encephalomyelitis and does not resemble the primary virus encephalitides, as exemplified by rabies, poliomyelitis and St. Louis encephalitis.

DISCUSSION

Dr. I. J. Sands, Brooklyn: For the past decade I have followed the neurologic material at the Kingston Avenue Hospital for Contagious Diseases. The cases are drawn from a population of approximately 3,000,000. Seldom, if ever, does true encephalitis complicate scarlet fever. A scarlatinal rash in Negroes is sometimes difficult to recognize, and frequently other types of rashes may be mistaken for the eruption of scarlet fever. I have known clinicians of long experience to disagree on the diagnosis of such a rash. Without intending to disparage the diagnostic skill of those in charge of this case, I reserve the right to question the original clinical diagnosis. The patient obviously had encephalomyelitis, but the cause was unknown.

Dr. Arthur Weil, Chicago: I am not quite as skeptical as Dr. Sands with respect to the clinical diagnosis in this case, but I agree with Dr. Winkelman that the histopathologic picture which he demonstrated is unusual for a case of encephalitis following scarlet fever. From the few cases reported in the literature and my own limited experience, it appears that metastatic, emboli-disseminated encephalitis may occur after infections of the kidneys, lungs and other organs. The condition may be accompanied by multiple small hemorrhages or by purpura of the brain. I cannot agree with Dr. Winkelman that the lesions in his preparations resembled those of encephalitis following measles. In the latter condition the gray matter is usually spared, while in the present case there was a massive

inflammatory reaction in both the gray and the white matter. Furthermore, with measles one usually does not see such severe meningitis and such pronounced perivascular lymphocytic infiltration; the perivascular gliosis and necrosis are more prominent in measles.

The term demyelination is rather loosely used in present day literature; frequently the author does not state whether there is disappearance of the myelin sheaths alone or whether the paling in his myelin-stained preparations indicates also a breaking down of axis-cylinders, a complete necrosis of the axon, as it may be seen in the perivascular foci of measles encephalitis in adequately silver-impregnated sections.

DR. N. W. WINKELMAN, Philadelphia: I agree thoroughly with Dr. Sands with respect to the difficulties of diagnosis of scarlet fever in a Negro child. In this case, however, the patient was examined at a municipal hospital where Negroes are treated in large numbers. The staff members were unanimous in their conclusion that the patient was suffering from scarlet fever and that the neurologic manifestations were the result of that condition.

Dr. Weil is correct in his statement that the complication of encephalitis in the course of scarlet fever is extremely rare; for that reason alone this case was made the subject of a special report. I am in accord with Dr. Weil in regard to the greater involvement of the white matter, but I do not entirely agree that the gray matter is usually spared. In most cases of measles encephalitis or of postvaccinal encephalitis there is some involvement of both the cortex and the subcortex. Globus (Infections of the Central Nervous System, *A. Research Nerv. & Ment. Dis., Proc.* [1931] **12**:33, 1932) stated that in the postvaccinal type of encephalitis "the inflammatory changes . . . show no preference for the white or gray matter."

I agree that the term demyelination is used loosely by most authors. In my case there were actual perivascular necroses to account for the loss of myelin sheaths around the veins.

New Staining Method for Demonstration of Debaryomyces Neoformans (Torula Histolytica), Blastomyces Hominis, Coccidioides Immitis and Histoplasma Capsulatum in Histologic Preparations. DR. J. W. KERNOHAN, Rochester, Minn.

This study was undertaken because of the difficulty of demonstrating Debaryomyces neoformans (Torula histolytica), Blastomyces hominis, Coccidioides immitis and certain other fungi in histologic preparations. Cresyl violet stains the capsules of these organisms pale sky blue and the contents of the capsule frequently rose or pink.

With Meyer's mucicarmine, Debaryomyces neoformans stains scarlet; the capsules of Blastomyces and Coccidioides immitis and certain other fungi are red, and the contents take a variable color but frequently do not stain.

With Best's carmine, the capsules and organisms stain a deeper hue, but since the background is also darker, the contrast is little, if any, improved.

With silver stains, these organisms are outlined sharply and are distinguished readily. I have counterstained the silver preparations with the carmine stain recommended by Best for the demonstration of glycogen. This combination of methods is superior to any I have encountered. The organisms (Debaryomyces, Blastomyces, Coccidioides, etc.) all stain scarlet and are sharply outlined with the silver. This combined stain also eliminates the pink or reddish background which is so objectionable with the Best carmine stain alone. The latter is apparently not specific for glycogen, but demonstrates in a characteristic manner amebas, certain yeasts and fungi, and so forth. In a recent case of infection of the heart valve with Histoplasma capsulatum the combined stain demonstrated the organisms clearly and differentiated them from the surrounding tissue. The cytoplasm of the organisms was scarlet and contained small granules of material impregnated with the silver. Furthermore, the organisms varied in size, from the small variety usually noted to very large forms. The latter resembled closely

large yeastlike bodies, and a few contained numerous small forms simulating endospores. On the other hand, some of the organisms of intermediate size were forming buds. This variation in size and form of H. capsulatum should be investigated by a competent and experienced mycologist.

DISCUSSION

DR. LEO ALEXANDER, Durham, N. C.: All who have struggled with the difficult problem of staining these organisms satisfactorily will be grateful to Dr. Kernohan for his important contribution.

DR. PERCIVAL BAILEY, Chicago: Watts, in a paper on Torula infection (*Am. J. Path.* **8**:167 [March] 1932) published from my clinic, showed that Masson's technic for mucicarmine is an excellent stain for yeast. The organisms stain red against a clear yellow background (metanil yellow).

DR. WALTER FREEMAN, Washington, D. C.: Dr. Kernohan has shown some exceptionally beautiful preparations demonstrating these parasitic invaders in the meninges of the central nervous system. It is admitted that ordinary hematoxylin and eosin preparations are unsatisfactory, and there is such a variation in the staining reaction of the organisms to thionine and so little of the tissue visible with the Gram stain that this method has its place. Personally, I have used the Perdrau silver impregnation method with rather satisfactory results; the organism shows up prominently.

Histogenesis of Cerebral Arteriosclerosis. DR. G. EROS, Orangeburg, N. Y., and DR. A. FERRARO, New York.

Our report deals especially with the histogenesis of the vascular changes in over 50 brains for which a clinical diagnosis of cerebral arteriosclerosis had been made. On the basis of our studies, we feel that the primary, and most important, changes take place in the elastic tissue of the blood vessels, especially in the so-called internal elastic membrane. All the other degenerative changes, such as fatty and mucoid degeneration, calcification, fibrous proliferation and hyalinization, are only secondary to the changes in the elastic tissue.

Two main types of degenerative changes can be distinguished: (1) the hyperplastic and (2) the hypoplastic.

In the hyperplastic degenerative type there is a pronounced tendency to proliferation of the elastic tissue in the larger, as well as in the smaller, arteries of the brain. The internal elastic membrane shows reduplication and multiplication even in the early stages. This hyperplasia of the elastic tissue is the primary factor and is at times accompanied by, or generally followed by, degenerative changes and fibrous proliferation of the intima.

In the first stage the newly formed elastic fibers and lamellas are darkly stained and sharply outlined, and the degenerative changes are not pronounced. Later the deposition of fatty substances is gradually increased and is accompanied by fibrous proliferation of the intima. In the more advanced stages the elastic lamellas and fibers become paler, their outlines lose definition and the deposition of fatty substances is particularly pronounced in the deeper layers of the intima. In advanced stages the proliferated elastic fibers and lamellas disappear, being partially or totally replaced by fibrous connective tissue. In these late stages there are usually conspicuous fatty and mucoid changes, hyaline degeneration and, eventually, deposition of calcium in the intima. The lumen of the arteries becomes narrower, owing to proliferation of the intima. As the pathologic process progresses, these proliferative and degenerative alterations gradually involve the other layers of the artery, especially the media.

In the hypoplastic degenerative type there is little, or no, tendency to proliferation of the elastic tissue. The elastic membrane is pale and indistinct in outline, even in the earliest stages of arteriosclerosis. Reduplication or multiplication of the layers of the elastic membrane is not evident. In later stages the elastic membrane is swollen, pale, loose and folded. In many arteries exhibiting this type of degeneration the internal elastic membrane seems to have undergone thickening, which closer study reveals to be pseudothickening, the result of

swelling of the degenerated elastic membrane. The swollen membrane is lacking in elastic substance. Fat stains may show fatty degeneration of the intima in the very early stages. These degenerative changes in the elastica in some arteries may be accompanied by moderate fibrous proliferation of the intima, but in many of the arteries no fibrous thickening of the intima or appreciable diminution of the lumen of the arteries is noticeable. On the contrary, the lumen is usually wider than normal, and the walls of blood vessels show deformities and indentations, presumably related to loss of elasticity. In more advanced stages the degenerative changes may gradually involve the other layers, with subsequent fibrosis, fatty degeneration or hyalinization of the entire wall. However, in these advanced stages some of the degenerated arteries remain wide open and do not disclose appreciable diminution of their lumen.

While this distinction between the hyperplastic and the hypoplastic type of cerebral arteriosclerosis holds true for the intracerebral blood vessels, the large arteries of the circle of Willis are likely to show a less evident difference because of their greater tendency to major proliferation of the elastic tissue and degenerative changes in the entire wall. Neither the hypoplastic nor the hyperplastic variety seems to be related to advanced age, inasmuch as the degeneration may appear in comparatively young persons.

Constitutional factors may play an important part in determining the type of reaction of the blood vesesls to all sorts of pathogenic agents. This contention is in support of the statement that arteriosclerosis is not a disease of advanced age only but is determined by the constitutional makeup of the vascular system.

In the hypoplastic degenerative type of arteriosclerosis diffuse vascular disturbances may deevlop, which may lead to diffuse parenchymatous changes rather than to circumscribed softenings. In the hyperplastic degenerative type the intimal proliferation and the diminution of the lumen of the arteries lead, rather, to various types of softenings and accompanying focal symptoms. In the hypoplastic type hemorrhages occur even in the early stages and appear more often than in the hyperplastic type. We have never encountered hemorrhages accompanying the hyperplastic type of vascular change except in the later stages, when severe degeneration takes place.

DISCUSSION

Dr. C. E. Benda, Wrentham, Mass.: Arteriosclerosis is a well defined clinical and pathologic entity, and general pathologists have been concerned to a great extent with the problem of arteriosclerosis of the arteries of the body. Of the pictures which Dr. Eros demonstrated, only a few showed what one would call arteriosclerosis of the cerebral vessels. The other slides presented various types of hypertrophic fibrosis of the arteries or atrophic and degenerative changes.

One might study the condition of the cerebral arteries in cases in which the general pathologist has recognized pronounced arteriosclerosis in the vessels of the body organs. Dr. Eros and Dr. Ferraro noted little arteriosclerosis in the brain in their investigation I doubt, however, whether the condition of the cerebral arteries was their primary concern, for Dr. Eros stated that they noted no relation between the age of the patient and the so-called arteriosclerotic changes in the brain. Examination of the cerebral vessels in cases of severe arteriosclerosis of the coronary and other arteries shows frequently little arteriosclerosis of the vessels of the brain; I was especially impressed in studies on paralysis agitans by the frequency with which the vessels in the brain were free from arteriosclerosis when the pathologist had reported advanced arteriosclerosis in the body organs. My experience is in accord with that of several other investigators.

On the other hand, I fear that the application of the term arteriosclerosis, which is well established in general pathology, to the changes in the cerebral vessels which these authors observed will lead to great confusion. Hypertrophy of the intima is seen in many conditions, especially chronic infectious diseases; if one studies the arteries leading to a tuberculous organ, one usually sees proliferation of the intima in that area. In most diseases of the brain the arteries react either

with hypertrophic or with degenerative changes, and in the brains of children 2 or 3 years of age I have seen changes similar to those the authors presented. In hardly a single case with pronounced pathologic changes in the brain did careful study of the cerebral arteries not discover considerable alteration of the vascular walls. If one is going to call all such changes arteriosclerosis, one will be confronted with a huge amount of arteriosclerotic conditions of the brain of various types. The term arteriosclerosis should be reserved for those conditions in which the vessels undergo primary degenerative metamorphosis, with fatty degeneration of the intima and media. Arteriosclerosis of the vessels of the brain does occur, although it is rare, and a study of conditions under which arteriosclerosis of the cerebral vessels is to be found would be of special interest.

DR. LEO ALEXANDER, Durham, N. C.: I am inclined to agree that the subtle changes which the authors described belong in the wider field of the lesions one is justified in calling arteriosclerosis.

DR. N. W. WINKELMAN, Philadelphia: I have always believed that arteriosclerosis is a clinical rather than a pathologic term. Some years ago Dr. Patten and I studied the blood vessels in a large group of patients over 50 years of age. We divided the changes in the blood vessels into three main types: first, the atheromatous change, which corresponds to the authors' hypertrophic degenerative type; second, arteriofibrosis, which corresponds to their atrophic degenerative type, and, third, hyalinization of the media, which occurs mainly in the medium-sized arteries, rather than in the large basal vessels.

We felt that our classification was important because it gave us some idea of the clinical picture. We found that patients with the arteriofibrotic type live to be older than did those with changes of the other two types. Many patients with the arteriofibrotic form showed no evidence of the usual senile mental changes that are so prevalent with the atheromatous type. With the latter type there was a tendency to hypertension, and the patients did not live as long as those with arteriofibrosis. Frequently the atheromatous type was associated with hyalinization of the medium blood vessels. It was among patients with this form of degeneration that the most severe hypertension occurred, with relatively short duration of life, frequently not beyond 50, and prominent mental and neurologic disturbances.

DR. I. M. SCHEINKER, Cincinnati: I do not agree with Dr. Benda's criticism or with his statement that the slides which were presented did not demonstrate arteriosclerotic changes. I believe that the preparations illustrate the most characteristic feature of the early stage of cerebral arteriosclerosis. As a matter of fact, degeneration of the media associated with circumscribed plaque formation, the criterion required by Dr. Benda, is not the characteristic change in cerebral arteriosclerosis. The seat of degeneration of the vessel wall in the vessels of the brain seems to differ from that in the vessels of other organs. Involvement of the media by plaque formation is exceptional in cases of cerebral arteriosclerosis, and therefore it cannot be considered characteristic. I agree heartily with the authors that the changes demonstrated in the elastic membrane and the proliferation of the intima are the most characteristic pathologic features of the early stage of cerebral arteriosclerosis.

DR. G. EROS, Orangeburg, N. Y.: According to present knowledge, arteriosclerotic changes in the cerebral vessels are represented by a combination of several characteristic degenerative and productive changes in the vessel walls. Arteriosclerosis is a well defined clinical and pathologic entity, as Dr. Benda states. Hyperplasia of the intima of the cerebral blood vessels other than the arteriosclerotic type, as well as deposits of simple fat in the intima and media, can be mistaken for cerebral arteriosclerosis only by one not familiar with the clinical, macroscopic and histologic manifestations of cerebral arteriosclerosis. We did not say that arteriosclerosis was represented in our material only by simple intimal hyperplasia of some cerebral arteries. On the contrary, we showed in our photographs the gradual development of the characteristic severe arteriosclerotic change from its beginning in the elastic tissue.

As our present contribution to the problem of cerebral arteriosclerosis is in the field of histogenesis, we have illustrated the first stages of arteriosclerosis, with special emphasis on the beginning and the advanced changes in the elastica, which, in our opinion, constitute the primary factor in the development of cerebral arteriosclerosis. For this reason, we have shown sections stained for elastic tissue which demonstrate that these changes in the elastica are generally uncomplicated at the beginning. Later, they are followed by other degenerative and productive changes in the arterial wall characteristic of arteriosclerosis. We were able to follow these changes from the early to the far advanced stages because arteriosclerotic changes are not the same everywhere in the same brain. In some regions of the brain such alterations may be severe, while in others they are only moderate, slight or just beginning. I wish to emphasize again that the cerebral arteries in all our cases showed various degrees of arteriosclerotic change, from very early, mild alterations to far advanced ones, accompanied by pronounced parenchymatous changes and by softenings of or hemorrhages in the brain substance. All our cases were clinically, as well as pathologically, instances of pronounced cerebral arteriosclerosis, with prominent mental or neurologic manifestations.

With regard to age, neither of the types described by us seems to be restricted to advanced age, and arteriosclerosis of both types can be observed in relatively young persons. We do not believe, however, that the changes in the blood vessels demonstrated by us could be observed in the brain of a 2 to 3 year old child. The terms, such as "marked alteration of the blood vessels," which Dr. Benda used in his comment on the changes in the blood vessels which he has observed in the brains of children, do not give a clear idea of his meaning.

Degenerative or productive changes in the elastica of the cerebral blood vessels, with splitting of the elastic membrane, can be detected in conditions other than arteriosclerosis, even in children. But these lesions cannot be mistaken for those of arteriosclerosis, in spite of the fact that the degenerative and proliferative changes in the elastica are important factors in arteriosclerosis as well.

Though it is true that the severity of cerebral arteriosclerosis is not always related to the severity of the arteriosclerotic changes in other regions and organs in the same person, we should not say that cerebral arteriosclerosis is a rare disease. On the contrary, because of its frequency, especially in older persons, it represents an important problem for the psychiatrist and neurologist.

Dr. A. Ferraro, New York: I, too, wish to emphasize that our presentation was intended primarily to illustrate the early stages of cerebral arteriosclerosis. We were not interested in demonstrating the end result of such a condition, in which productive and degenerative changes may lead to partial or total occlusion of the blood vessels; therefore, Dr. Eros' slides were intended to overemphasize our contention that the primary damage takes place in the elastic tissue. We could have shown dozens of slides illustrating the terminal phase of hypertrophic degenerative arteriosclerosis. Our conception of a primary pathologic process in the elastic tissue led us to distinguish two types of vascular reaction: one, in which primary hyperplasia of the elastic tissue dominates, and the other, in which primary hypoplasia and inadequacy of the elastic tissue constitute the initial vascular pathologic process.

On the other hand, all the brains in our series disclosed macroscopic indications of cerebral arteriosclerosis in the generally accepted meaning of the term, evidence confirming the clinical diagnosis of psychosis with cerebral arteriosclerosis. Our studies dealt principally with early stages of the vascular pathologic process leading to the typical macroscopic feature of arteriosclerosis.

This paper will appear in a future issue of the *Journal of Neuropathology and Experimental Neurology.*

Gliomatous Tumors in the Nasal Region. Dr. Edward W. Davis, Chicago.

Glioma is rarely encountered in the nasal region but is interesting from the standpoint of tumor genesis. The case of a child 6 months old who had such a

glioma at birth, anterior to the nasal bones, is presented. The tumor was composed predominantly of glial tissue with abundant blood vessels. Similar cases from the literature are briefly noted, and theories of the origin of the glioma are discussed.

This paper was published in the July 1942 issue of the *Journal of Neuropathology and Experimental Neurology*, page 312.

Vascularization of Cerebral Neoplasms Studied with the Fuchsin Staining Method of Eros. Dr. S. Arieti, Brentwood, N. Y.

This paper is a study by the fuchsin staining method (Eros) of the vascular pattern and morphologic characteristics of blood vessels in various types of cerebral neoplasms. Both the distribution and the morphologic characteristics of the vessels are considered. The vascularization of medulloepithelioma, medulloblastoma, spongioblastoma multiforme, unipolar and bipolar spongioblastoma, astrocytoma, oligodendroglioma and mixed gliomas was studied.

In the medulloepithelioma the angioarchitecture consists of a fine network of capillaries, very thin, and particularly numerous in the periphery of nodular nests of cells. In 2 medulloblastomas a fine, irregular web of capillaries and precapillaries was the chief vascular feature. The vascular pattern of the spongioblastoma multiforme consists of a central area almost deprived of blood vessels and of a peripheral part provided with numerous blood channels, varying from large sinusoids to channels of precapillary size, irregularly arranged, with beadlike deformities, looping and irregular branching.

The idea is advanced that from their vascularization it is possible to recognize a progressive maturity of the gliomas in agreement with the classification of Bailey and Cushing.

The importance of the abnormality of the vascular pattern in the mechanism of growth of the intracranial tumors and in their possible distant effects is stressed.

Fibroblastic meningioma exhibits large blood vessels entering the capsule. In addition, many minor vessels and capillaries are noted in the capsule and in the connective tissue septums dividing the tumor into irregular nodes. These blood vessels provide vascularization to the inner parts of the tumor. Minor vessels extend into the peripheral parts, and even to the center, of the cellular nodules. This distribution of the vessels, which seems to provide a fairly adequate supply of blood to the tumor, explains the infrequency of necrosis and cyst formation in fibroblastic meningioma. In angioblastic meningioma arborescent structures are the commonest feature. In the fibroblastic meningioma the vascularization is mostly capsular; in angioblastic meningioma it is mostly intracapsular.

Knowledge of the vascular pattern of these neoplasms may be useful not only from a morphologic point of view but in diagnostic arteriographic or histologic procedures. It may also contribute to a better understanding of the different mechanisms of growth in the various types of glioma. It is possible to recognize in several types of tumors a characteristic abnormal vascular pattern which undergoes progressive or regressive changes because of such factors as the distribution of its own elements, the compression exercised by them and the endarteritic processes. On the other hand, these changes in the vascular pattern may cause other alterations in the cellular components of the tumor. A vicious circle thus forms, which may lead to decay and necrosis of a great part of the neoplasm.

Furthermore, it must be stressed that the vascular changes mentioned and the resulting imbalance in hydrodynamics not only act within the tumor but often have far reaching effects.

Paraneoplastic engorgement of the pial vessels may result from transmission of the blood pressure from the tumor to other parts which are more susceptible to expansion than are the vessels in the relatively free subarachnoid space. However, one should bear in mind that in the normal tissue surrounding the tumor the blood vessels are often compressed by the contiguous neoplasm. As a matter of fact, fuchsin stains fail to show any structure in some parts of the paraneoplastic area. It is therefore possible that in many cases the dilatation of the meningeal blood vessels is related to the stagnation of the blood, which cannot reach non-

neoplastic regions that are compressed by the tumor. These considerations stress the importance of distant vascular alterations. Some of the neighborhood symptoms observed in cerebral tumors might be ascribed to them.

DISCUSSION

DR. L. ALEXANDER, Durham, N. C.: The author has completely confirmed the observation of Dr. Sahs and myself in regard to this interesting problem.

DR. A. L. SAHS, Iowa City: Several years ago Dr. Alexander and I (Sahs, A. L., and Alexander, L.: Vascular Pattern of Certain Intracranial Neoplasms: Studies with the Benzidine Stain, ARCH. NEUROL. & PSYCHIAT. **42**:44 [July] 1939) studied the vascular pattern of a group of intracranial neoplasms. I am gratified to know that our observations are confirmed by another staining method. The fuchsin stain has the advantage of being applicable to material which has been fixed for variable periods, while the benzidine stain must be used on relatively fresh material. With respect to the gliomas, one can say in general that the relative bizarreness and irregularity of the vascular pattern are a reliable index of the malignancy of the tumor.

DR. PERCIVAL BAILEY, Chicago: Neither the Eros nor the Pickworth method demonstrates the entire vascular bed, since they are methods for staining erythrocytes.

DR. N. W. WINKELMAN, Philadelphia: Has Dr. Arieti had the opportunity of studying by this method tumors which had been irradiated? I ask because I am interested in the action of radiation on tumors in general. Do the rays act directly on the tumor cells or through the medium of the blood vessels, and therefore the blood supply?

DR. S. ARIETI, New York: In answer to Dr. Winkelman's question, I did not have the opportunity of studying the vascularization of brain tumors which had been irradiated.

In answer to Dr. Bailey's comment, even though the Pickworth and Eros methods stain erythrocytes, comparative studies with vascular injections show the satisfactory visualization of the capillaries with the Eros method. On the other hand, fuchsin, which is used in the Eros method for less differentiated sections, stains the walls of the blood vessels also.

This paper was published in the October 1942 issue of the *Journal of Neuropathology and Experimental Medicine*, page 375.

Myoclonus Epilepsy: Clinicopathologic Report of a Case. DR. L. ROIZIN and DR. A. FERRARO, New York.

A girl aged 16 years first had convulsions at the age of 14 years, after an appendectomy. The character of the involuntary movements which were noticed in the course of unconsciousness, and in its absence, pointed to a clinical diagnosis of myoclonus epilepsy. The patient's brother died of the same condition, and a sister was admitted to the Craig Colony for Epileptics at the age of 15 years and died a year later of a streptococcic infection. Thus, the familial trend of the condition is established.

Histopathologic study of the brain revealed a large number of nerve cells with characteristic cellular inclusions, resembling the bodies described by Lafora under the heading of "amyloid bodies." Such inclusions were present in most of the cortical areas but were more numerous in the dentate nucleus and in the substantia nigra, the latter having practically lost its normal pigmentation. Several types of degenerative changes in the nerve cells were also observed in various areas.

Histochemical studies were carried out in order to establish the chemical nature and histogenesis of these cellular inclusions. The cellular inclusions usually gave a positive reaction for amyloid. However, in certain limited areas or in individual nerve cells the reaction was either completely negative or only partially positive. In other cells the inclusions gave only a more or less intensely positive reaction for hyalin, fibrinoid or carbohydrate.

Frequently the same cellular inclusion reacts positively to tests for various substances, such as fibrin or hyalin, with or without amyloid. This combination of various substances seems to have its equivalent in the appearance of the individual inclusion. Each concentric stratum of the inclusion may take a different reaction. Each layer gives only one reaction, the whole stratum being uniformly positive for one or another reaction.

In view of the complex nature of the amyloid substance and of the still debated phase of its development, one may speculate on the relation of the variation in histochemical reactions to the complex chemical structure of the body and the correspondence of the different chemical reactions to different stages of the development or metabolism of the amyloid substance.

This view seems to be supported, also, by the positive reaction of some of the inclusions to methods meant to detect carbohydrate and protein substances, which may constitute a link in the formation of amyloid.

In view of these morphologic and histochemical considerations, we believe that it is in the interest of precision to avoid the term amyloid bodies, and we suggest instead "heteromorphic inclusions," i. e., bodies differing in morphologic appearance or structure at different stages of formation.

An interesting feature of this case was the presence in the frontal lobes of a large area of telangiectasis. This telangiectasias, though more pronounced in the frontal lobe, affected scattered blood vessels in other areas, which appear dilated.

DISCUSSION

DR. G. B. HASSIN, Chicago: The cell inclusions were first described not by Lafora but by Bevan-Lewis in an epileptic idiot, in the second volume of *Brain* (1879). These structures are so commonly myoclonus epilepsy that one is tempted to identify them associated with myoclonic epileptiform contractions. I have seen them in vast numbers in a case of amaurotic family idiocy, the late infantile type of Jansky and Bielschowsky, of which only 6 instances have been recorded. The patient exhibited continuous clonic contractions of the eyelids and the muscles of the lower extremities, which did not subside even during sleep—veritable *épilepsie continua*. I consider the case one of myoclonus epilepsy in view of the sole presence of clonic muscular contractions. The inclusions were in the form of amyloid bodies, which stained brilliant green with toluidine blue and brown with the silver method of Bielschowsky. In fact, they could be stained by any method except that for amyloid. The inclusions were lodged within the cytoplasm of the nerve cells, and the nucleus was not involved. These bodies indicate a metabolic disturbance, as was assumed by Lafora, and may be considered to be what Alzheimer called *Abbau*.

DR. WALTER FREEMAN, Washington, D. C.: Relatively few of this kind have been reported, none that I know of in which so many methods have been employed, with such a revelation concerning the structure of these inclusion bodies and with presentation of so excellent an argument with respect to their nature. The very fact that these bodies have a concentric arrangement seems to denote a process of hysteresis, similar to that observed in the precipitation of insoluble salts in gels; yet the lack of any crystalline structure, as observed under the microscope, indicates that these intracellular bodies are highly complicated chemical compounds, certainly more than simple salts of iron, calcium and phosphorus. The exact nature of these inclusion bodies is by no means clear. There is no reason to believe that they are virus inclusions, nor do they seem to be associated with actual degeneration of the cell, since the nuclear membrane and nucleolus, although displaced, appear relatively normal. These bodies must, however, in some way interfere with the proper function of the nerve cells, in view of the obvious deteriorating nature of the disease and the peculiar motor manifestations.

Has Dr. Roizin any explanation for the fissured arrangement sometimes seen in these bodies? Has he observed them, as I have, deposited wholesale in the substantia nigra? Many years ago, at St. Elizabeths Hospital, Lafora described these inclusions, and I had the opportunity of comparing the sections in his case

with those in a case encountered in my own experience. The changes are so characteristic that the diagnosis is easily established.

DR. L. ROIZIN, New York: With respect to the spheroid bodies which Bevan-Lewis described within the nerve cells of the cortex in a case of "epileptic idiocy," one wonders whether these inclusions can be considered analogous to or identical with the amyloid bodies of Lafora, for in his description Bevan-Lewis expressed the opinion that they were granules, closely packed in the nerve cell from its apex to its basal extremity. In the absence of any detailed morphologic and chemical description, it is difficult to establish the analogy between these granules and the so-called amyloid bodies of Lafora.

I have had the opportunity of studying some of the cellular inclusions associated with amaurotic idiocy, which in my estimation did not resemble the so-called amyloid bodies. They consisted rather of granules of various sizes, which stained particularly well with safranin and resembled the so-called safranophil bodies described by Didé and Bogaert. It is of interest, however, to note that Dr. Hassin has observed amyloid bodies in nerve cells in cases of the late infantile (Jansky-Bielschowsky) form of amaurotic idiocy. The case of amaurotic idiocy to which I referred was one of the Vogt-Spielmeyer type.

In answer to Dr. Freeman's inquiry, at the present stage of the investigation I have no explanation for the fissured arrangement which is sometimes seen in these bodies. In our case we observed a considerable amount of cellular inclusions in the substantia nigra, which was one of the areas most severely involved.

This paper was published in full in the July 1942 issue of the *Journal of Neuropathology and Experimental Neurology*, page 297.

Changes in the Eyes in Amaurotic Family Idiocy (Infantile Type of Tay-Sachs Disease): Histopathologic Observations in a Case. DR. G. B. HASSIN, Chicago.

The eyes, together with the brain and spinal cord, in a typical case of amaurotic family idiocy, were removed sixteen hours after death.

The following conclusions are drawn from the study of this material:

1. The changes in the retina and optic nerves in patients suffering from amaurotic family idiocy are analogous to the changes in the central nervous system in general.

2. The perioptic spaces exhibit the presence of elements similar to those seen in the subarachnoid spaces of the brain and spinal cord.

3. The hyperplasia of the pial septums in the optic nerves is analogous to that of the pia-arachnoid and is a reaction of the latter to the presence of abnormal products of activity of the ganglion cells discharged there by way of the perioptic spaces.

4. Status spongiosus—a manifestation of severe destruction of nerve tissue—is a striking feature in the changes in the optic nerve associated with amaurotic family idiocy.

PHILADELPHIA PSYCHIATRIC SOCIETY

ARTHUR P. NOYES, M.D., *President, in the Chair*

Regular Meeting, Oct. 9, 1942

Value of Formal Psychiatric Examinations in the Criminal Court. DR. S. HARVARD KAUFMAN (by invitation).

The history of the role of the psychiatrist in the criminal court is reviewed, with consideration of the various shortcomings of the relation between law and psychiatry. The wider use of psychiatry and sociology in the juvenile court is mentioned as an example of the future role of the criminal psychiatrist. The need

of psychiatric examination of convicted criminals is indicated by the fact that many persons with psychopathic problems are, unfortunately, committed to the penitentiary and later have to be transferred to psychiatric institutions. The formation of an experimental court clinic is described, and 4 case histories are given to demonstrate the procedure employed in this clinic. Forty-two, or 29 per cent, of 146 persons sentenced in the court during the time this clinic was functioning were seen by the psychiatrist.

Various psychiatric problems are discussed. The value and limitations of psychiatric opinion in their solution are mentioned, and the hope is expressed that, in spite of the comparative inflexibility of the criminal law, a greater tendency toward the use of orthopenology and correctional therapy with the aid of psychiatric examinations in the court may come about.

Masochistic Motives in Criminal Behavior. DR. PHILIP Q. ROCHE.

Consideration is directed to the problem of self-thwarting trends and the "need of punishment" as often discerned in the behavior of criminals, especially in those who are parole violators and recidivists. Such self-abnegating trends and the attainment of punishment are reflections of "moral masochism," and they are more evident in the criminal character than is ordinarily suspected. Several aspects of the criminal behavior pattern are discussed. 1. Basically the criminal behavior is infantile and has its prototype in the asocial drives of the child. 2. The criminal act has a symptomatic kinship with psychoneurotic conflict, and it often represents a resolution of anxiety. 3. Humiliation, physical abuse and ostracism obtain for the criminal a masochistic gain and satisfaction similar to that which the psychoneurotic person attains in functional symptoms. 4. Punishment, like symptoms, seldom if ever achieves a desirable modification of the character, but tends rather to fix the criminal in his neurotic dilemma and to prevent him from gaining access to his inner conflict and self-thwarting drives. The author points out that the criminal is rarely able to give a logical explanation for his criminal act, as if he were as helpless as the psychoneurotic patient, who is unable to explain his symptoms. It is emphasized that the aim of the masochist is not suffering per se but the "forgetting of one's self," the obliterating of one's self in the effort to overcome the conflict engendered by one's helplessness, powerlessness and insignificance.

This paper was published in full in the *Journal of Criminal Psychopathology* (**4**:431-444 [Jan.] 1943).

DISCUSSION ON PAPERS BY DR. ROCHE AND DR. KAUFMAN

DR. HUGO STAUB, New York: For many years I have been interested in the relationship of the psychiatrist to the court, and I am pleased that much progress toward utilization of the psychiatrist in court proceedings has been made during the past fifty years. There has always been mild antagonism between the officers of the court and the psychiatrists, because the two groups speak different languages. The court is interested primarily in punishing the criminal in order to prevent future crimes, while the psychiatrist is interested in the criminal as a clinical problem. This has led to considerable disagreement, which is most noticeable when the psychiatrist is called on to discuss the criminal's responsibility.

The increased interest in motives, drives and emotional conflicts that has arisen from Freud's pioneer work in dynamic psychology has been of considerable value in clarifying the position of the psychiatrist.

I believe that much criminal behavior arises out of immature emotional reactions. The prison environment can be of little benefit in the treatment of such immaturity; as a matter of fact, it tends to increase the immaturity and dependence of the criminal by providing him with many of his basic physical needs. It appears, then, that the immature criminal should be placed in an environment in which he can grow up emotionally, and that in this respect the prison is quite useless.

DR. DAVID ABRAHAMSEN, Kew Gardens, N. Y.: It is important that society be educated to recognize normal and abnormal behavior. In general, it is easy to see that a man is psychotic, but it is difficult, for instance, to find the hidden traits behind the cool mask of the criminal. Psychiatrists have long been trying to get an insight into this problem, but much is left to be learned. All investigations, including such studies as Dr. Kaufman's, deserve attention. The ideal that all offenders be given a psychiatric examination is to be striven for. Under the present system this is impossible. However, there are two types of offenders, sex offenders and murderers, for whom a psychiatric examination before the court is of paramount importance. In Norway all such offenders are examined as a rule before they come to court.

Examination in court, might make possible, in addition more adequate individualization, proper placement of the offender. Since much crime is a result of immaturity, all criminals of immature type would, therefore, by proper classification be placed and educated in more suitable surroundings than the prisons. Even here it might be possible to provide education by psychiatrists and psychologists. For all these reasons, thorough examination of the offenders and greater collaboration with the court before trial would accomplish better results.

It may be that Dr. Roche is right in his assumption of the role of masochistic traits in criminal behavior, but it is difficult to understand how this can be in keeping with knowledge that masochistic and sadistic traits go hand in hand. True, in many cases the offender shows predominantly either sadistic or masochistic traits, but when sadistic and apparently less pronounced masochistic traits are present, or vice versa, one would in all probability find an interplay of the two components.

DR. JOSEPH C. YASKIN: Although I am not a student of criminology, some challenging statements made this evening were of interest to me as a neuropsychiatrist. As I understand it, Dr. Roche believes that masochism plays an important role in the psychopathologic makeup of the criminal. Dr. Staub believes that the psychologic condition of the criminal does not differ materially from that of the psychotic, the psychoneurotic or the neurotic person. From my study of the psychoneuroses, I have felt that masochism is a mechanism one can frequently detect in psychopathologic conditions of many kinds. I, therefore, feel that masochism does not play any primary role in the psychopathology of the criminal.

I do not believe that sordid early environment is an important factor in the development of the criminal. I cannot escape the observation that many such persons have certain fundamental difficulties, perhaps inherited. It reminds me of a child whom I began to observe at the age of 10 or 11 years and who, at the age of about 14, committed some pretty serious crimes. This boy exhibited no anxiety regarding his misdoings. I cannot forget the statement that Judge Brown made, "I am going to give this fellow a break, but no matter what you or I, or any one else, does for this boy, he is headed for the penitentiary." In this connection, Dr. Gerald H. J. Pearson, who studied the aggressive child, came to the conclusion that such a child exhibits trends not ascribable to environmental factors and not correctable by any form of therapy.

One cannot escape the conclusion that in handling criminals society needs jails, just as it needs hospitals for the mentally ill. I do not mean to convey the idea that the jail offers the best mode of treating the criminal, any more than I believe that the hospital for the mentally ill is the best place for treating the insane.

DR. DANIEL J. MCCARTHY: With respect to the relation of the psychiatrist to the court, the rigid attitude of the court and the test of the sane and the insane grew out of the laxity of the English courts, where so many persons were being relieved of the responsibility of their crimes. In the McNaughton case, the test of right and wrong was brought out, and agreement on the matter of mental disorder was reached. I agree that the whole problem of crime is one of mental disorder; certainly, it is a matter for the psychiatrist. For eighteen or twenty years Judge Brown, of the Municipal Court of Philadelphia, has worked on the

assumption that it is better that the judge have a complete knowledge of the case before, and not after, the trial, and that the offender be stamped as a criminal before that time. On the bench one wonders about the family history, the physical health, the environment and the psychologic factors. If the history is before the judge, he can ask intelligent questions of the attorney and is equipped with better knowledge before the matter goes to the jury. It is not sufficient to have the psychiatrist's judgment after the case is tried, and before the man is sentenced; the study should be made before the case is tried.

To go back to Dr. Roche's belief that one might solve the crime situation by educational and psychiatric means, one has only to sit in the court day after day to learn that some criminals are real criminals and that criminality is inherent in their protoplasm. But no generalized rules may be laid down; every case is different, just as is every case the physician studies in his office.

DR. SAMUEL LEOPOLD: The need of psychiatric examination in cases in the criminal court needs no argument. I am glad progress is now being made in this respect. Dr. McCarthy has so well expressed the views of the members on the subject that it is not necessary to repeat them.

The stress that Dr. Roche places on the masochistic motives in criminal behavior seems exaggerated. The average criminal is a practical man, in contact with mundane things, so that his feeling of guilt and need for expiation are, to say the least, very limited. I can see that there might be an occasional compulsive state with which masochistic behavior might be tied, but it is rare.

JUDGE CHARLES L. BROWN: Dr. McCarthy has overemphasized what my associates and I have been doing for a number of years. We do become familiar with the mental, physical and environmental conditions of children and adults who come into the social branches of our court. I have received many ideas from eminent physicians. At the time of the establishment of the Medical Advisory Board, Dr. Charles Penrose, the chairman, said to me: "Judge, I think you are doing a fine piece of work, but what of the physical and mental condition of those charged with crime and other offenses against the law? You do not know the first thing about the criminal that comes before the court. It is not possible to make an investigation of the environmental, physical or mental status prior to the trial. I suggest that, if at all possible, sentence be postponed until you can make such an investigation and submit your report to the judge as a guide in the passing of judgment." This we have been doing since 1917. Of course, I do not think one should become too tender about the punishment of crime. Society ought to be protected, and one should not be too morbidly interested in a man who is judged antisocial. Particularly, society should be better protected against the feebleminded delinquent.

JUDGE GERALD F. FLOOD: The court has used psychiatric assistance in a number of cases, I believe not more than 40 out of 100, and a great deal of good has come from the material. Quarter Sessions Court does not have such a service, but I believe that all agree that it should. At present, when my colleagues and I encounter a case of sex offense we are confused; we know little about the background and usually have to defer sentence until a psychiatric examination is completed. Usually the report is returned to us in a week, and in the meantime we have forgotten a great deal about the offense and the atmosphere of the courtroom while the trial was going on. The psychiatric examination is important, but I believe there is something much more important that has not been worked out in Philadelphia—the differentiation of institutions to which the offender is sent after judgment has been passed on him.

DR. PHILIP Q. ROCHE: At the outset, I should like to say that it is my intention to convey the idea that masochistic motives are more often the basis of criminal behavior than is commonly suspected. One is accustomed to think of crime in terms of criminal aggression against the public, and is less mindful of the criminal's aggression against himself. When one examines a criminal in terms of irrational aggression against himself, one comes closer not only to a more satisfactory explanation of the criminal act but to a more effective approach to

treatment. In my experience, I have rarely obtained an adequate explanation for his act from the criminal or from the court, which has imposed punishment on him.

In this presentation I also emphasized that physical symptoms and misbehavior are but variants of the same psychic conflict, and I pointed out that their development at the threshold of parole, and often during parole, is not accidental, but is a meaningful indication that punishment alone has not secured the criminal against himself.

I surmise from comments of the discussants that my thesis proposes a soft indulgence of the criminal. I propose the abolition of punishment as a measured revenge of the community, but I do not propose that one do away with segregation. I propose that the criminal be segregated in the same way that the psychotic patient is removed from free circulation in the community, and that his restoration to the community be dependent not on a predetermined sentence but on nonjudicial agencies trained in the task of human appraisal and in the technic assisting the criminal (or the psychotic patient) in modifying his impulses to those within community tolerance. In this proposal I visualize the principle of the indeterminate sentence of the criminal as it is now, in effect, applied to the insane. In either case, one is dealing with a socially disabled person.

CHICAGO NEUROLOGICAL SOCIETY

ARTHUR WEIL, M.D., *President, in the Chair*

Regular Meeting, Oct. 15, 1942

Function of the Frontal Lobe in Man: The Dynamic Visual Field. DR. WARD C. HALSTEAD (by invitation).

The dynamic visual field is that portion of the peripheral retinal field that can be made to yield a threshold visual impression at the same instant that a form discrimination is being made in the region of the fovea. It has been mapped in normal persons and in carefully selected patients with unilateral neurosurgical lesions who had no ocular disturbance. For exposures as brief as twenty to fifty milliseconds, the dynamic visual field was found to correspond with the campimetric field in normal subjects and in patients with a large lesion of the occipital or the parietal lobe with associated hemianopia. Patients with a lesion of the frontal lobe had normally full campimetric visual fields. Their dynamic visual fields were greatly constricted, however, even when exposures as long as eighty to one hundred milliseconds were employed. For certain types of visual situations it may thus be demonstrated that the patient with a unilateral lesion of the frontal lobe has available quantitatively less visual field than the patient with homonymous hemianopia associated with a large cerebral lesion posterior to the frontal lobe. The relation of this observation to results which other investigators and I have previously reported is discussed.

This paper will be published in full.

Encephalitis Associated with Herpes Zoster: Report of a Case. DR. SIGMUND KRUMHOLZ and DR. JOSEPH A. LUHAN.

A housewife, aged 58, who had previously been in fairly good health, on March 7, 1942 had severe pain in a cutaneous area, which two days later became the seat of a herpetic rash, limited to the lower part of the face, the neck and the upper part of the shoulder and chest on the left side. A dermatologist confirmed the diagnosis of herpes zoster. On April 5 the patient became mentally disturbed. Examination the next day by one of us (S. K.) revealed she was moaning and restless and out of contact with the environment. The rectal tem-

perature was 104.6 F. The lungs were clear. Although the patient was uncooperative, there was no detectable paralysis of the cranial nerves or the extremities, and the reflexes were normal. The spinal fluid contained 40 cells per cubic millimeter, 80 per cent of which were lymphocytes. The patient continued to be noisy and restless; and her illness ran a febrile course, and she died on April 15, ten days after onset of the cerebral symptoms and thirty-nine days after appearance of the zoster.

Necropsy revealed fibrinous pericardosis, advanced parenchymatous degeneration of the myocardium and terminal bronchopneumonia. The spinal cord was not obtained. Histologic examination of sections from many blocks taken from all lobes of the brain, the subcortical white matter, the basal ganglia and the hypothalamus revealed only edema and hyperemia of the leptomeninges, "acute ganglion cell disease" in the cortex and a hydropic state of the white matter underlying the ependymal surfaces. The medulla, on the other hand, was the seat of a meningoencephalitis, characterized by (1) mild perivascular infiltrations of lymphocytes; (2) tissue foci, principally in the olives and the cuneate nuclei, containing numerous microglial polyblasts and showing cellular destruction, neuronophagia and capillary hyperplasia, and (3) small patches of demyelination, especially near one of the olives. The pons and midbrain appeared to be uninvolved.

The noninfiltrative changes in the cerebral cortex were like those seen in some cases of toxic encephalopathy. The question arises whether both these lesions and the anatomically demonstrable nonsuppurative meningoencephalitis inferior were produced by one etiologic agent, the virus of herpes zoster. It is reasonable to ascribe the medullary process to upward dissemination of this neurotropic virus, which entered the cord through the cervical roots.

DISCUSSION

DR. MAURICE OPPENHEIM: When I saw the patient on April 5, in consultation with Dr. C. R. Windmueller, she was in bed, screaming, extremely restless and in poor general condition in consequence of lack of food. There was no doubt of the diagnosis of herpes zoster, which had been made by Dr. Windmueller. On the left side, the lower part of the face, the neck, the pectoral area and the scapular region were involved. Red spots of various sizes, with scars in the center, were noted. Six weeks after onset the herpetic blisters were entirely gone, and the subsequent nervous condition developed. Dr. Krumholz agreed with me in suspecting encephalitis.

Three forms of herpes are encountered in dermatologic practice, of which two are often confused, herpes zoster and herpes simplex zosteriformis; herpes simplex is easily diagnosed. It would not be surprising to see encephalitis follow herpes simplex, for experimental studies on rabbits have shown that the infection can spread to the cord and involve the brain. Herpes zoster is clinically different: many crops of blisters follow in succession. The infection cannot be transmitted to the cornea of the rabbit. Herpes zoster also shows complement fixation with the serum from blisters of herpes zoster, whereas herpes simplex does not. Patients with herpes zoster usually recover, without relapse; with herpes simplex they frequently succumb.

Many authorities believe that herpes zoster and chickenpox are caused by the same virus, and it is known that chickenpox is sometimes followed by encephalitis. Bokai was the first to advocate this hypothesis. Osler reported cases in which encephalitis followed the final stage of chickenpox.

In the present case the herpes zoster had entirely disappeared six weeks after the onset. My first impression was that the nervous complication was meningitis, which sometimes follows herpes zoster. This case could be used as proof of Bokai's theory that chickenpox and herpes zoster are caused by the same virus—the herpetic virus, a neurotropic and dermotropic virus. It may be, therefore, that herpes zoster in some cases is followed by encephalitis. In postvaccinal encephalitis, which may occur nine to thirteen days after vaccination, the virus

belongs to the same group. This case was a typical instance of herpes zoster, and not of herpes simplex zosteriformis.

DR. GEORGE B. HASSIN: I do not understand how one can associate herpes zoster with cerebral manifestations that occurred weeks after its onset. In Thalheimer's case the interval was six weeks, and for this reason some authorities do not consider it one of herpetic encephalitis. In the case I observed the cerebral symptoms were coexistent with a herpetic eruption along the distribution of the fifth nerve, and it has been shown experimentally that encephalitis can be produced in rabbits by inoculation of the cornea with herpes virus. Kuttner, among others, emphasized that herpetic encephalitis differs from the epidemic type and that it is a specific morbid entity.

The changes in the brain in this case have been well demonstrated by the authors, who stressed the edema and perivascular infiltrations in the medulla. The edema was much more pronounced than the infiltrations and generally, in my opinion, is of greater importance than changes in the vessels or the ganglion cells. The condition of the subependymal areas and the ventricles themselves should be of great interest.

Eonism: Report of a Case with Additional Outstanding Psychopathic Features. DR. D. M. OLKON and DR. IRENE CASE SHERMAN.

An outstanding type of sexual abnormality is eonism, or transvestitism. Many investigators have reported cases from history, from police records and from their own experience, under a variety of designations referring to the same type of personality anlage. Hirschfeld's *Transvestite* was classified by Krafft-Ebing under fetischistic personality; Havelock Ellis called it eonism, or sexesthetic inversion; by still others it has been included under the caption of homosexuality. All designations, however, are for the purpose of establishing the psychopathic trends in the personality.

A case history was given; the patient's autobiography was read, and photographs were presented. Physically, the patient was normal. His hair was long, well groomed and carefully waved. He had worn women's clothes constantly for the past seven years. By psychologic tests his intelligence rating was average. The results of the Rorschach test were indicative of a compulsive neurotic personality. He asked to be certified as a female and to have his genitalia amputated and a vagina constructed.

Terminology in this case was inadequate, as the patient presented many more abnormalities of personality than his dressing in female attire. The novelty was the multiplicity of tendencies, which could hardly be understood from orthodox designation. He showed evidences of narcissism, exhibitionism, fetishism, masochism and sadism and was homosexual. In addition, he was lacking in emotional response and social sensitiveness, showed no evidence of shame or regard for the opinions of others and rejected all responsibility to society. This dichotomy of trends makes the case unique.

DISCUSSION

DR. IRENE CASE SHERMAN: The patient was referred to the Illinois Neuropsychiatric Institute from the draft board, after having appeared there in female attire. Physically he was normal in every respect. The physical proportions were of masculine type; the chest was broad, and the hips were narrow. The distribution of hair, also, was masculine. The skin was rather fine, but the hair was of average coarseness. He was proud of his hair and had it waved at a beauty salon regularly. The only occasions on which he had been arrested were when he was in male attire, because the long hair attracted attention. When he went about dressed as a woman, he was not apprehended.

His intelligence quotient was 95. In the Rorschach test he gave an unusually large number of responses, with a great deal of detail. This was interpreted as indicative of a compulsive-obsessive type of neurotic personality. There is little

information on the dynamics of his behavior. Assays of the hormonal content of the urine were not made, because he refused to cooperate. He is much opposed to any glandular treatment because he wishes to be a woman.

DR. RALPH HAMILL: I do not know about diving into this whirlpool of the question of boy and girl. I have worked about twenty years with children, and I have concluded that every boy wants to be a girl and every girl a boy. As I interpret it, the boy takes with a great deal of chagrin the fact that the girl can have a baby and he cannot. Every boy up to the age of 12 whom I have been able to get close to has told me he wanted to be a girl; that is so surprising that I have tried to think of some reason. As far as I can explain it, every boy gets used to his own body and wants to know about another kind of body, and the only way to know it is to be it. Consequently, the matter gets out of the realm of sex and into that of knowledge.

It seems to me that this fact is an important element in mental disease. After puberty, when function has determined what structure has only suggested up to that time, the idea is ridiculous. But the ridiculous is the crazy, an important element in schizophrenia. It is a remnant of childhood that gets into the sexual field, and one can ridicule it; nevertheless, it is important.

Book Reviews

Lectures on Conditioned Reflexes: Volume II. Conditioned Reflexes and Psychiatry. By Ivan Petrovitch Pavlov. Translated and edited by W. Horsley Gantt, M.D., B.Sc. Price $4. Pp. 199. New York: International Publishers, 1941.

This volume contains all of Pavlov's lectures on conditioned reflexes from 1928 to his death in 1936. With volume I (1903 to 1928) the English reader has a complete collection of Pavlov's lectures on this subject. Gantt has done the difficult task of translation with credit. Moreover, he has written a twenty-eight page introduction, in which he discusses the history of Pavlov's research and gives a critical evaluation of his work. Best of all is the appreciation of the man himself, in the section entitled "Closing Years." Here one senses what a really great figure Pavlov was—his energy, his enthusiasm and his ability to plan. In 1935 he told the International Congress in Moscow: "I am an experimenter from head to foot. My whole life has consisted of experiments." And in 1936, in a letter to young scientists, he insisted on the importance of systematic planning: "From the very beginning of your work, train yourselves to be strictly systematic in amassing knowledge."

The main body of the book is composed of fifteen lectures on conditioned reflexes or the application of the principles of conditioning to psychiatry and psychology. The best of the lectures are those dealing with his own physiologic work, summaries that bring out his discoveries and principles, such as chapter XLIII, "A Brief Outline of the Higher Nervous Activity," and chapter XLIV, "Contributions to the Physiology and Pathology of the Higher Nervous Activity," and his own story of the investigations and concepts in chapter LVII, "The Conditioned Reflex," written in 1935. These are important contributions from a great man that should be in every library of neuropsychiatry.

Pavlov is at his worst when he speaks of the clinical field. As Gantt says in the translator's preface, "It is not the fortune of many to explore a fresh field of inquiry after the age of seventy-five." In this he tells of his explorations into the domain of psychiatry—perhaps it was a misfortune. Although he is tentative in his writing, as in chapter XLII, "Trial Excursion of a Physiologist in the Field of Psychiatry," he sometimes makes bold statements on what to a clinician would seem like inadequate evidence. For instance, "studying the aforementioned schizophrenic symptoms, I came to the conclusion that they are the expression of a chronic hypnotic state." With somewhat more reason he connects hysteria with hypnosis (chapter LII). In chapter LV, "An Attempt at a Physiological Interpretation of Obsessions and of Paranoia," he shows that he has read extensively on paranoia and describes some cases, admitting frankly that he is no clinician. He wishes merely to bring out that "psychiatrists in their respective domains, will inevitably have to reckon with the following fundamental pathophysiological fact: the complete isolation of functionally pathological (at the aetiological moment) points of the cortex, the pathological inertness of the excitatory process, and the ultra-paradoxical phase." To accept this point of view at all one must believe that brains may be "strong" or "weak" (neither of these terms is sufficiently defined) and that the cortex is made up of a mosaic of interrelated excitatory and inhibitory points.

Mental Health in College. By Clements C. Fry, M.D., with the collaboration of Edna G. Rostow. Price, $2. Pp. 365. New York: Commonwealth Fund, Division of Publications, 1942.

This book is a useful effort directed toward altering of the policy of the more backward institutions of higher education the student health services of which do not yet include those of a psychiatrist. It should prove helpful to the college dean, the bewildered parents of an errant college youth, the teacher who wonders why some students may fall far short of the promise given, the psychiatrist interested in adolescents or the campus physician who finds no clue to troublesome symptoms.

Dr. Fry has been associated with Yale University in the capacity of psychiatrist since 1926. The material of the book draws on the case histories of 1,257 students seen by the student health service during the ten years prior to 1942.

Approximately half the volume is concerned with problems of personality growth, divided into two chapters, the first dealing with problems of family relationships and the second with sexual growth, behavior and attitudes. College students, however, are a special group of adolescents, subjected to the peculiar strains of the university, with its characteristic organization, traditions and mores. In his dealing with problems of this order, the object of the psychiatrist is in a general sense an educational one, for he is interested in furthering the growth of the student's character.

Another portion of the book concerns itself briefly with reactions to the undergraduate environment. It deals with a description of the complexities of organization of Yale's various schools, the college plan and the social significance of fraternities, senior societies and honor societies. Scholastic adjustment and social adjustment are dealt with at greater length, and, as always, principles are illustrated admirably with case histories. To know that many maladjustments are inevitable when any group of persons tries to adjust to a new environment should serve as incitement to discovery of personality difficulties among students as early as possible in order that the psychiatrist may assist individual students to achieve a satisfactory adjustment and thereby increase their efficiency and the productivity of their college experience.

The last section of this volume deals with the problems found in the graduate and professional schools. Dr. Fry speaks deprecatingly, in small print, of the therapeutic effects of psychoanalysis seen in a small group of students, and wistfully, in larger print, of the peculiar resistance of medical students to psychiatry. The author is deeply appreciative of Dr. Adolf Meyer's influence in the development of his psychobiologic approach to these problems of mental hygiene.

The book is recommended for college physicians.

Love Against Hate. By Karl Menninger, M.D., with the collaboration of Jeanetta Lyle Menninger. Price $3.50. Pp. 311. New York: Harcourt, Brace and Co., Inc., 1942.

In the introduction Menninger states that he deliberately chose to write this book for any intelligent person, professional or nonprofessional, rather than for the specialist. He states, however, that the substance of his book is what he teaches his students and discusses with his colleagues. In my opinion, the book is readable, the style is polished and the content is of value not only to the lay public but to professional persons, including other psychiatrists. The purpose of the book is to show the resources which one has at one's command to favor the life (love) instinct and to oppose the death (hate) instinct. In the first four chapters the author describes the frustrations of the child, the frustrations of women and the deprecation of femininity. The chapter dealing with frustrations of the child is well presented and contains material widely accepted by the psychiatric profession. In the chapter on frustrations of women, Menninger points out that women frustrate their children because they themselves have been

frustrated by civilization in general, and by men in particular, by means of political, economic and legal codes which keep them in abeyance. They are frustrated frequently in their sexual life and are often deprived of the experience of pregnancy and childbirth. In a subsequent chapter, the author points out ways in which a woman identifies herself with the male aggressor and then depreciates her own femininity.

In the second half of the book the author suggests five solutions for these problems, namely: work, play, faith, hope and love. Each of these five topics is described at some length in the individual chapters. Work is described as being of the greatest importance as a method of absorbing the aggressive energies of mankind in a useful direction, and the author points out ways in which work can be pleasurable. He emphasizes the need of vocational education and the failure of most psychiatrists and analysts to support these aims. In the chapter devoted to play, he describes various play technics used with children and adults with mental disorders and illustrates recreational outlets for normal persons in card playing, dancing, art, music, etc.

The book contains many short but valuable case histories and has an adequate bibliography. In my opinion, the book is to be highly recommended.

Our Age of Unreason. By Franz Alexander, M.D. Price $3. Pp. 341. New York: J. B. Lippincott Company, 1942.

This book is an attempt by a psychoanalyst to understand and explain the chaos of the present day world.

The volume is divided into three sections, entitled "Reason to Unreason," "The Fundamentals of Human Behavior" and "From Unreason to Reason." There is a 130 page survey of the world's history, particularly that of Germany, as well as a brief survey of the philosophies and psychologies of the various countries at war. These summaries are superficial. At one point the author emphasizes the need for psychoanalysts who are physiologists, historians, anthropologists and sociologists and who will apply psychoanalysis to the study of biologic and social processes. Any one entitled to consider himself a specialist in such a wide field of interest would be a rare person. The need for such persons is real.

It must, however, be noted that the book is a sincere attempt to approach the problem of world chaos from a new viewpoint in order to explain the irrational behavior of the world. The author relates the nationalistic irrational behavior of some countries to the unconscious aggressions which are never expressed in a totalitarian state. He indicates that in the development of Germany there was a rapid change from a feudal to a modern industrialized national state, all in a historically brief period. This led to a paternalistic attitude, which suppressed all hostile impulses in the individual. These impulses, in turn, were directed outwardly against other countries. In a democracy, with its slower development and freer play of emotions, there is less inner tension in the individual, and therefore less need for destruction of a neighboring country. For the layman, the book offers a different interpretation of the present day world situation. For the student of neurology and psychiatry, it is a superficial study.

Introduction to the Psychoanalytic Theory of the Libido. By Richard Sterba. Nervous and Mental Disease Monograph Series, No. 68. Price $2. Pp. 81. New York: Nervous and Mental Disease Publishing Company, 1942.

The author feels that psychoanalysis faces a real danger, for he sees in the "culturalist school" a disregard of the libido theory, which he considers one of the basic concepts in freudian psychoanalysis. It is with this thought in mind that the book is written as a "timely recapitulation" of Freud's observations concerning the instincts. It appears to us that this book has a *raison d'etre* more plausible than as a defense against attacks on the libido theory. For one who has

read the basic material on instinct and libido, there is nothing new in this book. However, for the beginner who would like some more continuous presentation of the libido theory than he would get if he went to the sources, this book serves a useful purpose. One would get the impression from the preface that the author planned to take up the cudgels in defense of the libido theory, but one finds no pro and con presentations in this book, and other theories and viewpoints are not discussed.

The author presents in a simple and clear style the freudian concepts of instincts, with special attention to the sexual instinct. He discusses the various well known phases of development of the libido, utilizing Abraham's modifications. In addition, there are chapters on narcissism, the viscissitudes of the instincts and, finally, the repetition compulsion and the death instinct. All of this is presented in a readable and simple fashion. The book would have benefited considerably by having a good bibliography.